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Precaution and Ethics
Handling risks, uncertainties and knowledge gaps in the regulation of new biotechnologies

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1. Introduction

1.1 The commission

This report is a result of a commission by the Swiss Federal Ethics Committee on Non-Human Biotechnology (ECNH) to provide an analysis of ethical issues in the introduction of new biotechnology in the non-human domain, with particular focus on the application of a precautionary principle. This work was carried out starting November, 2016, with a draft outline approved late December the same year, and a first full draft submitted April, 2017. This draft was presented and discussed with the ECNH at a workshop in May, and the final report was then submitted in June 2017.

1.2 The topical area of the report

The topic of this report is defined by three key concepts: biotechnology, non-human domain and ethical issue. I will here provide an explanation of these three notions that will also serve as an explanation of the boundaries of the report. *Biotechnology* is understood as any kind of controlled human action to effect biological change of organisms or natural systems. *Non-human domain* indicates that whatever organism or natural system a biotechnology is applied to, its primary interference does not *immediately* interact with a human being or a human social system. However, a biotechnological action in the non-human domain may (and will probably always) nevertheless have indirect effects on human beings and human social systems. *Ethical issues* are issues about what is good or bad, desirable or undesirable, permissible or impermissible with respect to such biotechnological actions. These ethical issues can arise for singular human agents, such as a farmer or a scientist, for organised human groups, as well as for private and public institutions. Thus, although ethical issues tend to regard very different

actions and become more complex when addressing the political level of human decision-making, they nevertheless remain ethical in the same sense of regarding what is acceptable and desirable to do or not to do. Below, I will elaborate somewhat further on these explanations, to further clarify what this report tries to do and what it does not try to do.

The use of biotechnological interventions applied to other living things than human beings, especially those having an impact on genetic features of organisms or populations of organisms, have been contested in various ways for a long time. Our contemporary debates tend to have their origins in the initial worries formulated by scientists in connection to the emergence of the hybrid DNA technology in the 1970's (what we usually call "gene technology") and other methods based in laboratory science, e. g. with regard to military applications or environmental consequences (Bennet et al., 2013; Dyson & Harris 1994). However, for a much longer time, human beings have been using various other means to change the genetic composition of organisms, species or larger populations, more or less intentionally and with varying degrees of control. Similar methods have been applied to effect desired outcomes that are not immediately about genetic composition, but nevertheless are about achieving an outcome where an organism, a species or a piece of nature functions in a way that match some human desire. These methods include mutation stimulation, breeding and crossing, modification of environmental conditions of habitats, and moving of organisms or species between geographical locations. Also these methods have been subjected to critical discussion, e. g. with regard to their effects on the well-being of animals and humans, the features and function of natural systems, or the fit to existing human practices and values, in areas such as farming, fishing, forestry or other industrial trades using elements of natural systems (Blatz 1991; Resnik 2013; Thompson & Kaplan 2014).

The difference between these strands of biotechnology (in the non-human domain) are partly about their origin, partly about at what level of biological or physical function the method applies its interference to achieve some result. Gene technology and related "lab science"-based methods interfere at very basic levels, meddling directly with core mechanisms of life, procreation and the composition of physical matter. The other methods have originated

in long-standing practices independently of science and, although they may today use scientific knowledge of basic biological mechanisms as a background to application, they typically interfere on less finely granular levels to effect the desired result, or interfere with much less precision on some basic level. For this reason, in everyday thinking, some of these actions are not thought of as "technological" at all, as this epithet has come to be associated with sophisticated scientific methods with high levels of precision in the public mind. However, both families of methods are just as technological both regarding what they attempt to do (control nature for human purposes), and with regard to their panorama of potential effects. As I have understood the commission of this report to address *general* ethical concerns that may arise due to biotechnology in the non-human domain, I have therefore found no reason to exclude any of these types of biotechnology.

This is of particular importance when bearing in mind recent developments in gene technology, such as so-called gene editing and gene driving, both emerging as a result of the new biotechnological innovation called CRISPRcas9 (for a useful overview, see Nuffield Council of Bioethics 2016). While precision genetic modification before had to leave what laws governing gene technology refer to as "foreign genetic material" (or similar expressions) in the modified organism, these new applications hold out even more effective and precise modification of the genome of organisms and species without any such side-effect, more or less mimicking the basic mechanisms of natural mutation processes, only better controlled. In addition, the new technologies can be applied to effect rapid and precise change not only of a single organism, but of an entire population, and not only in a controlled laboratory setting, but in a complex natural system, and also here without leaving any traceable "foreign" genetic material behind. This "gene driving" may be applied to introduce also traditionally modified organisms (e.g. through induced mutation, crossing or breeding) in a natural setting, which illustrates how technologies for genetic control and design of organisms are becoming increasingly difficult to distinguish from the traditional technologies, or natural processes. This means that we may increasingly have organisms with modified genomes and entire populations of such that will not at all be regulated by current laws and systems for control of genetically

modified organisms (GMO) (Eriksson 2015). However, the ethical significance of introducing new genetic variants in nature, and to change natural systems genetically and otherwise, have not in any way changed with the arrival of the new methods (Kim & Kim 2016). A vivid illustration are very recent debates around the notion of using gene edited mosquitos, rapidly introduced in nature through gene driving, to combat the spread of the Zika virus in South America, the Caribbean and the southern United States (Glenza 2016). If we look even further into the future, and consider possibilities opened by synthetic biology and bionanotechnology, the notion of a GMO or similar ideas of "manipulated" parts of nature being especially fit for regulation lose its sense, as the products of such biotechnological engineering are rather fit to describe as uniquely manufactured objects and organisms, which are in no way "variants" of existing species. But, clearly, the ethical challenges posed by such scenarios do not disappear with such semantic shifts, and neither do the ethical reasons for society to be able to regulate the introduction and use of such biotechnological applications.

This regards especially when the ethical issues are focused on the aspects highlighted by what is often called "the precautionary principle". The details of what such a principle may imply will be discussed in section 1.4 and chapter 3 below, but already here it may be stated that an ethical focus on precaution means primarily a focus on the responsibility of ascertaining that actions taken achieve good effects and avoid bad effects, or at least avoid bad effect that are out of proportion. Such considerations can arise in any area, but are particularly pertinent when actions involve interaction with complex systems, such as populations of organisms, natural ecosystems, landscapes, and so forth, where human ability of foresight and control is limited (Resnik 2013). It is this very limitation, rather than what exact interaction take place and what precise actions that facilitate it, that creates the need for particular consideration of what is known regarding long-term effects and side-effects, and what is responsible to do or not to do in light of that. Thus, the ethical issues considered in this report will primarily regard this aspect of biotechnology.

1.3 Ethical stances to biotechnology in the non-human domain

Biotechnology has elicited a number of ethical responses that may be grouped into thematic categories. Here follows one way of thus sorting positions to gain extra overview. The point of this map is to use it for exemplification in later discussions, as well as for more clearly positioning the ethical issues related to precaution in relation to other themes in the ethics of biotechnology.

1.3.1 Taboo or degree?

One especially salient variation is that between positions that advocate absolute or very strong bans on particular biotechnological interventions, and those that do not place any biotechnological intervention completely out of bounds morally. The latter as a rule instead present a number of morally relevant factors, which may determine what ethical reasons there are for using or not using the interventions in particular circumstances or situations. The idea of what those factors are, as well as what may ground absolute bans, may vary, and then invoke one or several of the competing ideas mentioned below regarding anthropocentrism, naturalness and responsibility.

1.3.2 Anthropocentrism or not?

This ethical theme is about what base of values and other moral grounds of appreciation should be applied when assessing biotechnological applications. Simply put, should such assessment consider only their involvement of and effects on human beings, or also other sorts of entities, independently of how they affect human beings? The idea that only human beings matter ethically is often called "anthropocentrism", and within it can be found a number of rivalling ideas of what the human good consists in more exactly (Brülde 1998), as well as the complex issue of our responsibility for effects on future people (Meyer 2016). Positions that challenge anthropocentrism range from various versions of the idea of animal moral rights (Armstrong & Botzler 2003) over to more or less ambitious ideas in environmental ethics that confer moral value to living organisms in general, to systems of such organisms (such as

species and biotopes), and/or to complex units of such systems in interaction with each other and non-living parts of nature (such as ecosystems and entire biospheres) (Brennan & Lo 2016).

1.3.3 The relevance of naturalness

One issue that repeatedly divides ethical responses to biotechnological applications has to do with what significance is put on a supposed distinction between natural and artificial ways of interfering with nature and natural processes. One idea is this kind of distinction is ethically fundamental, often in a way assuming that the human transformation of something natural into an artefact is always something bad. But it is, of course, also possible to apply familiar ideas of the value of human nature, to forward the idea that the artefact will always gain some extra value through the human interference making it possible. Another aspect of invoking this kind of distinction is to sort the products of human endeavours into those that are less ethically problematic (as they are "natural") and others that are problematic (due to their "unnaturalness"), which poses fundamental challenges due to the status of humanity as a part of nature (Andersson 2007). Due to this, and as making this distinction in one consistent way may often prove challenging, making arguments in terms of naturalness highly liable to conceptual confusion (Siipi 2008), many ethicist instead problematize its ethical importance (Birnbacher 2012; Van Haperen et al., 2012). Recently, this has led to critical perspectives on policy practices, e. g. related to food marking (Sandin 2017).

1.3.4 Risk, responsibility and precaution

This theme, as already hinted, relates itself to the fact that biotechnology often interferes with processes not fully understood, or involves interaction with natural systems understood only partially, or permitting only partial control of what outcomes result from such interaction. For this reason, no matter how well intended and, in those terms, ethically well motivated a biotechnological application may be, it may nevertheless turn out to be suboptimal, counterproductive and yield unforeseen negative effects. This implies that there are immediate questions of how cautious one

should be when introducing and using a new biotechnological application, but just as well regarding the responsibility of continuing using already established applications and methods in view of possible long-term hazard and possible less dangerous alternatives (Björnsson & Brülde 2017; Munthe 2011, 2013, 2016). This theme is peculiar in that it adds a special dimension to all other ethical discourses: for any type of possible ethical up- or downside of a biotechnological application in terms of violating bans or not, or the presence of ethically bad- and good-making factors, there is an additional question of how to proceed responsibly when knowledge about such other ethical factors is lacking – as such, in precision or in certainty.

This last ethical theme is the one that is in focus in the present report. This means that large segments of the ethics of biotechnology that regard the themes of anthropocentrism and naturalness and are otherwise often at the centre of discussion will be sidestepped. At the same time, whatever view is suggested within those themes regarding what is ethically good, bad, required or impermissible, the issues regarding responsibility and precaution can be added on as a special ethical dimension that is actualised in most if not all real cases of biotechnological application. The issue of whether principles for responsible precaution should take the form of absolute bans or have a more gradual form will be briefly touched on, but as all arguments seem to support a preference for the latter, the analysis that follows will mostly occur under a non-taboo assumption.

This theme of the *ethics of* precaution needs to be distinguished from more general legal and political discussions of a *precautionary principle* (PP). The idea of PP is often unclear, and there exist many different ways of implementing it at different levels of policy or in law (Sandin 2004; Steel 2014; Trouwborst 2002, 2007). It has been stressed how this multitude of levels in law and policy-making has made the notion of PP "absorb" what has been known as "the preventive principle", thus addressing both how known risks are to be handled, and how uncertainties regarding possible risks are to be handled (Trouwbortst 2009). The *ethical* issue with regard to all such regulative suggestions is, however, the same: how they can be justified. It is at this level that the notions of the ethics of responsible handling of risks and uncertainties appear. To spell

out what an ethically justified precautionary policy would amount to, we need an account of what is an ethically responsible way of handling risk and uncertainty in general. This justification can be distinguished from more concrete policy and legal principles employed within it, some of which may be called "precautionary principles". For simplicity's sake, I will for the most part of this report talk in terms of the ethics and/or philosophy of PP, and/or the ethics of risk and/or precaution, and then always mean the underlying ethical issues needed to be addressed to justify any of the political and/or legal norms often called PP. In the next section, the basic questions that need to be addressed in the pursuit of such an ethical justification are briefly introduced. A more specific and detailed description of what the ethics of risk and precaution involves follows in chapter 3.

1.4 The ethics of risk and the problem of knowledge gaps

The responsibility and precaution theme of the ethics of biotechnology thus actualises a peculiar dimension of ethics and underlying moral philosophical theory, in the emerging philosophical literature in this area often referred to as *the ethics of risk and uncertainty* (Asveld & Roeser 2009; Munthe, 2013; Hansson 2013). For this reason, a large portion of the more in-depth ethical analysis of the responsibility and precaution in this report will address central issues in this area of moral philosophy. To make the reader of this report keep the main nature of these issues in mind, I will here briefly introduce them in a non-technical way.

1.4.1 Responsible balancing of chances of benefits and risks of harm

This is the most familiar aspect of the ethics of risk and uncertainty, linking ethics closely to areas such as risk analysis, decision theory and cost benefit analysis. Assuming any sort of idea of what balance of benefit and harm of human action may be ethically acceptable, we can always ask how to proceed when there is some degree of uncertainty about what balance would in fact result from different options. Underlying issues that are actualised here will regard how to assess the relationship between extreme likelihoods

and values at stake, such as when there is a very small risk of very large harm in relation to an almost certain but modest benefit, or when chances of benefit and risk of harm are distributed very unevenly between potentially affected parties (Hansson 2013). For instance, the possible benefits of a new herbicide tolerant biotechnological crop may mostly be about (ethically speaking) minor economic gain befalling the company selling this crop and the linked herbicide, while the risks of harm (e. g. of resistance development of weeds) may be more substantial and potentially affect a much wider set of stake holders. Another central issue from the perspective of precaution regards if risks and benefits are to be viewed as ethically "on a par" or "symmetrical", or if a smaller risk of harm may be seen as morally more important than a potentially larger benefit (Munthe 2011, ch. 5).

1.4.2 Assessing the ethics of risking immoral action

Sometimes, the risk benefit panorama of a decision with imperfect information will include the possible upshot of a clearly moral or immoral outcome or action being among the consequences of an option. For instance, a risk that someone is wrongfully killed, that goods are distributed unjustly, or that rights are infringed. A familiar instance of this phenomenon is found in the so-called "social argument" against certain forms of (selling) GMO, where a risk of unjust exploitation of farmers (and sometimes consumers) is held as a reason against such forms. Likewise, it is sometimes argued that use of some types of GMO, such as the so-called golden rise or crops made to need much less herbicide or pesticide than other crops, would possibly include morally mandatory elements, such as performing a duty of care for people in need, or caring for the environment. (Høyer Toft 2012). Structurally, the ensuing risk ethical issue is very similar to the one about balancing chances of benefit with risks of harm, only now less easy to fit into a familiar comparative cost-benefit structure of the sort used in standard risk analysis. How, for instance, should the downside of a possible unjust exploitation of a number of farmers voluntarily using a commercial GMO that reduces the need for herbicide use below that allowed in ecological farming be balanced against the possible reduction of environmental harm resulting from such use. While

harms and benefits may always be compared across affected parties as some type of quantities that come in more or less, immoral or morally required action lends itself less readily to such analysis, making familiar structures from cost- benefit-, and risk analytical models less readily applicable.

1.4.3 The problem of knowledge gaps

A central risk ethical dimension of precautionary thinking is about how to proceed in cases when the basis of information for assessing the responsibility of a new application or practice is found lacking – when there is a "gap" in the knowledge required for making a defensible decision. One aspect of this ethical dimension is about *what* amount and quality of knowledge would suffice for making a defensible assessment, one that could ground a responsible decision. This issue often appears when a new technology or a substantially developed application of a known technology appears, and in the biotechnology area there are several examples of having scientists themselves decide to halt technological application while assembling more basic knowledge of its basic mechanism, and the way it may work in a more complex context than an isolated laboratory. This regards the famous 1975 Asilomar moratorium on live applications of the then pristine recombinant DNA molecule technology (Berg 2008), but also the recent statement from an international summit on human application of gene editing technology (Cicerone et al., 2015), urging caution in all clinical applications, especially in the germ line. Even more recently, calls for strong caution on the particular application of gene editing called "gene driving" (where a genetic variant, modified or not, is made to spread very quickly through a population) have been voiced by scientists and academic societies, and outright global bans have been considered (but rejected) by a United Nations meeting on biodiversity (Callaway 2016; Ledford 2016; National Academies of Sciences, Engineering and Medicine 2016). However, all such decisions to "delay while looking for more and better knowledge" also actualise a more tricky issue regarding how to determine when the knowledge gap has been sufficiently closed or narrowed for responsible decisions to be possible. This issue is known in the more basic research field of decision theory to present fundamental problems

for standard models applied in risk analytical methods, as there may always be reason to "update" the basis of any risk assessment, or ethical assessment, due to the fact that human knowledge is always imperfect and possibly mistaken.

1.5 Ethics, policy and regulation

The focus in the commission actualising this report is on the ethics of regulating the introduction of new biotechnologies. This means that the concentration will be on a systemic level, where the ethical assessment is meant to regard entire regulative systems. This makes for a different shape of the ethical analysis than if the topic had been the ethics of particular biotechnologies or biotechnological applications. An ethically defensible regulatory system may have to accept that some single instances are handled inadequately (within a generally adequate system). This may mean that singular biotechnological applications that would be *in*defensible when considered on their own may be *allowed* by an ethically defensible system of rules. But it may also mean that singular biotechnological applications that would be *defensible* – even desirable – will be *disallowed or impeded* by a nevertheless ethically defensible regulatory system. As other parts of law and policy, regulation for introducing new biotechnologies needs to be assessed as a whole, and not based on the idea of perfectly handling each single application.

At the same time, the ethics of assessing particular technologies or applications is not unimportant for assessing such a system of rules. Any regulatory system must take into account in which direction to err, in view of the fact that no system will be perfect. Thus, it is still of interest to consider factors of relevance for the ethical (precautionary) assessment of single technologies and applications of these, and try to have the system be sensitive to relevant differences. However, as the system is supposed to deliver its main good by its function all things considered, assessing it ethically also needs to consider structural considerations that sometimes create stark conflict between the assessment of single cases and collections of such.

For example, in debates and regulation of GMO, there is often no discernable distinction being made between, e. g. the commercial farming of GMO crops and the selling of products containing

ingredients from such farming. At the same time, clearly, there is an immense difference in terms of precaution between the action of growing GMO crops in open fields, and selling products made from the harvest of such operations. These aspects will be more clearly set out in the next section, but no great expertise is needed to understand that the former activity creates much more and more serious risks and uncertainties that the latter one. Moreover, having a single country banning or restricting the sale of a particular GMO-based goods will usually not affect the risks and uncertainties of GMO farming. However, a regulation that systematically impedes the introduction of GMO-based goods on consumer markets may be thought to have some such effect, as it structurally undermines the financial basis of GMO-farming, thus providing a political-economical incentive to have less such farming and less of the risks and uncertainties that it brings.

From the point of view of an ethics of risk and precaution that looks at the function of an entire regulatory system, the question then becomes whether the level of limiting risks and uncertainties expressed by this system as a whole is defensible or not. That way of looking at the problem has been a main concentration of some recent contributions to the philosophy of precaution (Munthe 2011, ch. 6; Steel 2014, ch. 9). In addition, regulatory systems actualise pragmatic considerations that might complicate the impact of some ethical considerations. These aspects will be addressed at the end of section 3.

2. Biotechnology in the Non-human Domain

As mentioned in section 1.2, the topical area of this report is rather wide regarding what may be considered to be a biotechnology (in the non-human domain). In that context, some selected examples were given for the purpose of illustration, but in this chapter, I will provide a more systematic account of different technologies to consider. This account is systematic in two ways. First, I will suggest a rough typology of biotechnologies, based on how they interfere with natural processes, related to aspects that are of particular relevance from a responsibility and precaution standpoint. Following that, I will work through a large number of biotechnologies, based on a chronological principle in terms of "traditional", "emerging" and "futuristic", thus including also a number of technologies which today are merely or mostly on the drawing board, saying a little about how they are of interest from a precautionary standpoint. I will then close by relating these two sections to each other, and chart the "domains of uncertainty and ignorance" actualised by different types of biotechnology.

2.1 A typology of biotechnological interference in nature

Based on what was said above regarding what about biotechnologies in the human domain makes them particularly interesting from a precautionary ethical standpoint, it is possible to roughly distinguish different dimensions regarding how different technological applications interfere with natural systems. Such a classification will, of course, not settle any ethical question, but may help the mind grasp what particular types of challenges of a precautionary ethical nature are actualised in different cases. It is important to note that this typology is not a strict taxonomy, where different categories are meant to be binary (either an application is in it or not) and mutually exclusive. On the contrary, the typology I propose is based on the idea that the functional features of a biotechnology that are of interest from a precautionary ethical standpoint are *always* present, but to a greater or lesser extent. Thus, they should be perceived of as dimensions within which biotechnological applications (in the non-human domain) significantly vary and differ as well as resemble each other.

These dimensions are:

2.1.1 Granularity (of utilised physical mechanism)

This aspect is about how the technological intervenes in a process to effect an outcome in terms of the level of the natural organisation of matter. For instance, an intervention that interferes with the interaction between different molecules is less granular than one that interferes with the very structure or composition of such molecules at the atomic level. Even more granularity would result if the interference instead took place at a sub-atomic level, while less granularity results as interventions interfere with super-molecular structures of greater and greater physical complexity. Extremely low granularity would be exemplified by many traditional biotechnologies, such as redesigning landscapes, moving species and breeding.

The relevance of this dimension from a precautionary ethical standpoint is that it links to our background knowledge, and abilities to understand and predict how an intervention would work. Interventions at more granular physical levels usually combine the features of addressing aspects of physical reality more closely to the front of basic scientific research, but also easier to study scientifically in a controlled way. At the same time, such study as a rule becomes very much harder, when an intervention at such a level is performed outside of an isolated laboratory setting, as a more granular level of mechanism has a greater potential for interactions and synergies in complex systems. A lesser level of granularity, in contrast, may allow better opportunity to study the compound overall effects of some intervention, although research on how observed effects are actually produced at a more basic level may then become many times less accessible for human understanding.

Granularity also links to our ability to control and possibly limit the effects of a biotechnological intervention. On the one hand, higher granularity often facilitates laboratory applications that may be isolated from surrounding natural systems, which affects reversibility (see below), using different types of barrier solutions (Jebari 2015). A known and very often applied barrier solution in the biotechnology area outside of research is to make organisms unable of natural procreation, so that they become easier to isolate

from a surrounding complex natural system. However, higher granularity at the same time creates increasing physical difficulty of having applied barriers effect such isolation. An extreme example from outside biotechnology is what it takes to isolate radioactive particles from nuclear power plants (which applies the very granular technology of controlled nuclear fission) from the surrounding environment. Likewise, the more the biotechnological application will have to be in interaction with complex natural systems to produce whatever good that it produces, the more difficult and costly it will be to apply barrier solutions to mitigate and control risks in actual use of the technology. Again, the often applied barrier of GMOs to be sterile (so that they cannot produce offspring) has the considerable cost of undermining the cost-effective farming practice of having one and the same operation producing both the harvest and the seeds for the next one. Such cost increases and related balancing of risks and benefits may lead to difficult line drawing problems. For instance, in basic biological plant research that apply gene technology to produce controlled variants to compare in situations resembling a natural environment (such as an experimental field or garden), barrier solutions such as the removal of buds or sprouts may or may not be seen as a sufficient mitigation of possible risk. Likewise, a biotechnologically manufactured crop that could significantly reduce needs to artificial nutrition and use of pesticides that is also sterile to minimise environmental risk becomes much less valuable for farmers and the environment, as only those farmers that can afford it will be able to continuously buy new seeds from the producer every year.

2.1.2 Complexity (of system interacted with)

This dimension is not about the type (and implied difficulty or potential for understanding) of interference utilised in a biotechnological application, but about what kind of object this interference is applied to. Less complexity as a rule implies better potential for understanding the outcome of a particular application, other things being equal. Higher degree of complexity also usually means more room for very large scale effects (good as well as bad).

Typically, the least complex systems that a biotechnology interacts with are the ones found when the technology is applied in

a basic research situation. Here, the aim is usually to minimise complexity, and control all forms of potential confounders of observed experimental outcomes, in order to be able to advance basic scientific knowledge. In contrast, an intervention such as gene editing an organism and then use gene driving to have this organism replace established members of the same species in nature (e.g. for purposes of disease prevention, or environmental intervention to mitigate toxic waste), or geoengineering interventions to completely transform a landscape to have it deliver other "eco-" and "nature-services" than before (e.g. store carbon dioxide, or shield potentially very dangerous materials, such as high level nuclear waste) will directly interact with a very complex system.

2.1.3 Width and longevity (of potential effects)

Different biotechnological applications will have different potential effects (and side-effects) on smaller or larger parts of nature. For instance, interventions that would involve introduction of very mobile organisms (such as wild species of airborne animals) would have a greater potential to have wider effects, rather than effects restricted to a limited geographical area, compared to introduction of plants adapted to very specific types of habitat. Likewise, some applications will have more potential for having effects that stretch over long time-periods than others, where (germ line) genetic changes are often used as an example of the former, as they include utilisation of natural reproductive systems to have effects propagated without any further intervention.

Both these aspects are relevant in two ways. First, increased width and longevity implies that whatever good or bad comes out of the application, there will be more of it, than if the effect had been more limited across space and time. Secondly, the same increase normally brings with it decreased potential for prediction of the effects.

2.1.4 Reversibility (of outcome)

This aspect is about the extent to which it would be possible (and practically feasible) to reverse the foreseen and unforeseen effects of a biotechnological application. This is of relevance as reversibility may make it less irresponsible to introduce a technology

with uncertain and potentially hazardous effects. At the same time, reversibility may often require costly arrangements, e. g. for long-term monitoring of how an application of a technology proceeds over time, and capacities for intervention to effect the reversal standing by. This may make reversibility practically infeasible due to unacceptable costs, although it may be possible to achieve in principle. Sometimes, of course, reversibility may not be possible at all.

In general, the prospect of reversibility tends to be better the more simple the mechanism interfered with, the less complex the system it is applied to and the lesser the width and longevity of its effect. It seems to be most readily accessible in the basic research situation, where an application may usually be tightly controlled (and this is also desirable for scientific reasons).

2.1.5 Holistic understanding (of actual causal context)

This aspect is neither about the technological mechanism nor about the object it applies to nor its effectiveness in whatever upshot is produced. Rather it is about the position of the agent utilising the technology, in terms of what possibility there is to understand what may happen as a result of applying the technology in a set reality, and to foresee good as well as bad effects in order to assess whether this would be good or bad "on the whole". While ability to understand isolated details of a technology (such as its primary physical mechanism, or expected outcome on one variable among many others, or the expected effects of a singular instance or product) is, of course, a part of such a "holistic" understanding, it is not sufficient for it. Holistic understanding needs to include an ability to grasp the overarching effects of introducing and using a whole family of instances/products that all apply the same technology.

Ability of such understanding is of fundamental importance from a precautionary standpoint in two ways: First, since it will indicate the potential for serious knowledge gaps. Second, since lack of holistic understanding will usually indicate less ability to control the outcome of the use of some technology. Both these aspects are very important when assessing what use of a technology can be viewed as ethically responsible in view of risks and uncertainties.

Note that the real causal context of a biotechnological application will always include not only natural mechanisms and systems, but also human and social factors (such as political, legal and economic ones) that affect how a technology will play out in reality (as opposed to on an idealised drawing board). For example, it has recently been discussed whether or not the marketing of herbicide tolerant GMOs, combined with agricultural economic mechanisms, may lead to "monocultural" practices of crop and herbicide use that increase the risk of weed resistance development, although GMOs "as such" have no effect of this kind (Perry et al., 2016). Another example is the apparent fact that, despite a theoretically strong potential for other, more obviously generally beneficial applications, a combination of political, legal and economic factors have resulted in actual applications of genetic modification in farming being concentrated to commercial production of infertile herbicide and pesticide tolerance crops, sold in combination with said toxins (Munthe 2011, ch. 6).

One thing of great relevance regarding this dimension is that it is highly dynamic – our ability to (holistically) understand a biotechnological application may be improved over time, through careful research, as well as documented practical experience. But such improvement may also be more or less difficult to effect, and that is by itself of relevance from a precautionary ethical standpoint. At the same time, discharging whatever understanding we have in a precautionary ethical decision-making may be impeded by institutional arrangements overly focused on the assessment of particular instances of application or single products. This is illustrated by the common systems for assessing GMOs (e.g. in the European Union), where this is prescribed to be undertaken for one singular instance or product at the time, while the overall effects of using an entire family of similar products (e.g. glyphosate tolerant GMOs) in real socio-economic circumstances across a larger territory and a longer time is left unexamined. As a side effect, there are no incentives for developing better holistic understanding in this area. Changes to such institutional arrangements may improve the prospect of holistic understanding, as well as it being actually discharged in policy making.

2.2 Traditional biotechnologies

In this subsection, a number of biotechnological applications and practices with a longstanding establishment in current human practices will be briefly presented. Concentration is on aspects of interest from a precautionary ethical perspective, using the typological dimensions set out in section 2.1.

2.2.1 Manipulating macro structure: soil, landscape, nutrition, light, temperature and air

Since the rise of human, settled civilisation, people have been manipulating different macro-aspects of nature to promote yield in farming, hunting, collection and related practices. Moving, processing and fertilising soil to promote growth, engineering food for domesticated animals, arranging landscapes for the purpose of more effective farming or hunting, reverting streams and constructing canals for drying up land, provide water or facilitate fishing, building sheltered areas for growing sensitive plants or simulating climatic conditions not accessible naturally, assembling natural materials (forestry, mining) for the production of tools, purpose specific refinement (e.g. construction materials) or other gadgets, and so on. All such traditional technological applications typically occur at a very low level of granularity, necessarily involve interaction with highly complex systems, often produce effects in nature that are lasting and widespread and very difficult to reverse (at least when we talk about widespread practices over long times), and for the most part of human history undertaken with a severe lack of holistic understanding. Today, this understanding is better and includes many dear lessons from a large number of unfortunate side effects, but on a whole our knowledge is limited to our experience of earlier examples, and most projections for novel attempts of this kind will be seriously limited.

2.2.2 Moving, recreating and eradicating types: species, habitats and landscapes

This is another ageold biotechnological practice, where human mobility and migration has also involved the movement of large pieces of nature. This regards organisms and species – domesticated as

well as wild – into entirely new territories where they would most likely not have appeared by themselves. It also involves the recreation of entire habitats for organisms and species valued by human beings, where the technologies and applications mentioned in the previous paragraph are often involved. As a part of such endeavours, humans have often eradicated naturally established species, biotopes and/or landscapes. Also this technology interferes at a very low level of granularity, albeit involving much interaction with very complex systems, producing effects in nature that are lasting and widespread and very difficult to reverse. For the most part, such practices have been undertaken without much holistic understanding. Nowadays, we know much more about how actions like these may produce undesirable systemic and long-term effects, but again the reliability of projections is undermined by the stark limitations of our actual documented experience. This lack of understanding is illustrated by recent research on the consequences of domestication of animals, e.g. in fish farming (Bolstad et al., 2017).

2.2.3 Breeding and crossing

The primordial genetic technologies for producing new variants of organisms and species, these practices have been as widely and longstanding used, and with a similar range of application, as the two types of practices mentioned earlier. The level of granularity of breeding and crossing is, however, higher, as they occur at the level of individual organisms and species, rather than complex systems of many organisms and other macro-ingredients in nature. Nevertheless, as most plants and animals thus produced are farmed and kept in a way that is unbarred from surrounding nature, this technology tends to interact a lot with very complex systems, and their outcomes tend to be both widespread and longstanding. However, reversibility is better here, as new unwanted products may simply be destroyed and to the extent that old variants and species are preserved and can be re-introduced. At the same time, variants that are spread into nature will have effects there that are usually not possible to undo. Regarding understanding, this has evolved over time, and nowadays breeding and crossing is often based on biological scientific insight to optimise the outcome, using genetic testing and typing and background knowledge about hereditary

patterns and the linkage between genes and phenotypical features. Otherwise, holistic understanding becomes increasingly limited the more a new variant produced differs from variants in nature that we have been able to study.

2.2.4 Artificial mutation production

While traditional breeding and crossing uses naturally existing genetic variants, growing insight that these are due to mutation and into how mutation is driven in natural systems has led to a practice of artificial mutation production, using radiation, toxic exposure and/or viral infection to induce mutation, and genetic testing technology to check for when a desired outcome results. This adds a significantly new ingredient to breeding and crossing, as it facilitates the manufacturing of genetic variants not found in nature (although they could arise spontaneously). This technology interferes at a significantly higher level of granularity than all of the previous ones. As it is applied in the context of breeding and crossing, it will moreover interfere with complex natural systems, and have widespread and longstanding effects to the same extent as those technologies. It offers a similar room for reversibility, except that the manufacturing of mutations is even easier than breeding and crossing to isolate from surrounding systems, in order to control whether or not produced outcomes are allowed to interact with nature or be destroyed. The fact that artificial mutation production is an outcome of increased scientific knowledge in physics, genetics, molecular and general biology, and engineering advances related to these fields, means that it is undertaken with more understanding than the more traditional technologies, but the holistic understanding may not be much better, as this regards the actual effects throughout natural and human social systems.

2.2.5 Genetic modification (old style)

This is the technology we know as genetic modification, based on the idea of cutting, adding or moving parts of the DNA-molecule, using recombinant DNA technology. As it has been around for more than 40 years, and is widely used throughout research, agriculture, forestry and fishery, and production industry (e. g. in

the pharmacological industry) it has now reserved the right to be termed traditional, albeit it is the latest in a long history of developmental steps since human beings started to manipulate the biosphere for their own ends. While many effects of genetic modification applications can be attained also through breeding and crossing, especially when combined with artificial mutation production, genetic modification technology usually offers a faster and more efficient route to the desired end. But it also facilitates outcomes that are not available using the traditional gene technologies, in particular the movement of genes and resulting transfer of phenotypical functions between very different species, such as resistant to different temperatures or potential threats such as bugs, parasites or toxic compounds. The level of granularity is here the highest among the traditional biotechnologies, as it interferes *within* molecules, compared to the acting *on* molecules in the case of (traditional) artificial mutation production. Depending on what exact application of the technology is being made, it may interfere with complex natural systems, and have widespread and longstanding effects to the same extent as those of the earlier technologies. However, it offers even better room for reversibility, as the initial product may be isolated from surrounding systems, and the technology itself offers the opportunity of "changing back" whatever outcome has been achieved. The high level of granularity at the same time means that such isolation may require rather elaborate and costly arrangements to achieve effective barriers. Once a product has been introduced in nature, reversibility is reduced. Genetic modification technology also illustrates a further step in the understanding behind its use, especially in view of the mentioned Asilomar moratorium on live applications (see section 1.4) that both stimulated and allowed for an uncommon degree of knowledge acquisition before use. At the same time, also here, holistic understanding is rather limited, as it depends rather little on the knowledge about the micro mechanistic aspects of the technology.

2.3 Emerging biotechnologies

The run through of different types of biotechnologies now moves over to less established ones, several currently existing mostly or entirely on the theoretical drawing board, in highly experimental

forms, or in only very early stages of use. Concentration is also here on aspects of interest from a precautionary ethical perspective, using the typological dimensions set out in section 2.1.

2.3.1 Genome editing

Genome editing is a recent breakthrough that both helps to achieve a number of desired endpoints of earlier technologies, such as breeding and crossing, artificial mutation production and genetic modification, in a much more precise, effective and controlled way than before, and also facilitates entirely new outcomes, such as gene driving (see next paragraph). Often exemplified by the CRISPRcas9 technical concept, there are also a number of other technical solutions available for genome editing, and in the future may very well emerge many more that are even more reliable, precise and speedy (Nuffield Council of Bioethics 2016). What is of particular interest is that gene editing technology may allow for precise and effective artificial mutation production (by effecting exact deletions of very small parts of a genetic sequence, thereby reliably and precisely boosting or shutting off very specific cellular functions) that is more effective and accurate than traditional genetic modification technologies while leaving no trace behind of such interference, thereby being indistinguishable from the way in which genetic changes in organisms and cells are being produced artificially using traditional techniques or spontaneously in nature. It also can boost the precision and effectiveness of *adding* entirely new components into a genome, regardless of where these come from – other organisms of the same species, other species, or synthetically produced genetic material (see below). Therefore, the level of granularity of genome editing is the highest of all biotechnologies to have emerged so far, possibly rivalled by nanotechnological applications (see below). Like with traditional genetic modification technology, the immediate product of a genome editing attempt may be isolated from complex natural systems and controlled inside laboratories, thereby offering opportunities for limiting the width and longevity of outcomes and providing room for reversibility in such settings. However, the precision and effectiveness of genome editing makes no difference to these aspects once a resulting organism or species has been put into contact with

a complex natural system, which it has to if it is going to be used for anything else than basic research. The level of understanding seems to be better than when the traditional genetic modification technology was introduced, but once again holistic understanding is as limited as before. In this case, a particular aspect that has been highlighted, is the apparent ease with which genome editing technology may be envisioned to be used in autodidactic "do-it-yourself" settings (so-called *biohacking*), entirely outside of regular systems for licensing and control related to science, agriculture and industry (Ledford 2015; Nuffield Council of Bioethics 2016).

2.3.2 Gene driving

Once a desired genetic variant has been confirmed in an organism, to make use of that fact it remains to have this variant spread throughout a species or geographically restricted population within a species. Due to the nature of natural heredity and reproduction, this can take a lot of time and include many sources of error and inaccuracy. Gene driving is a biotechnology aimed to get around such hurdles, and have a particular genetic variant quickly and effectively propagated throughout a population of organisms without the downsides suffered by other methods, such as the loss of genetic variation effected by cloning. While the gene driving mechanism itself is facilitated by genome editing (to effect changes that make the desired genetic material being evolutionary favoured), it can be applied to any organism that contains any type of genetic variant due to any type of source (natural mutation, breeding or crossing, artificial mutation production, traditional genetic modification or gene editing). The level of granularity of gene driving equals that of genome editing, but as the driving itself includes the introduction of a modified organism into a population for reproductive purposes, it necessarily includes more interaction with systems of a complexity depending on the nature and circumstances of the population in which the gene driving is effected. At the same time, gene driving shares with all the modern gene technological applications (from breeding and crossing and onwards) the possibility of isolating early steps of the procedure from surrounding complex natural systems, where effects will be potentially very widespread, longstanding and irreversible. If such isolation is not effected, these

dimensions are immediately affected, and to the extent that gene driving is added to some other genetic intervention, it will drastically increase how widespread, longstanding and (ir)reversible its effects are. The very feasibility of gene driving depends on a good level of understanding of the mechanisms involved. However, like before, holistic understanding decreases as the effect-range of a particular application increases, and the worry around "biohacking" may be added also in this case.

2.3.3 Synthetic biology

While (traditional) genetic modification and gene editing offer many opportunities for re-arranging genetic components already present in nature, the field of synthetic biology aims for a further step: to be able to technologically engineer organic systems out of inorganic components, thereby facilitating the production of organisms and organic components that have never before been present in nature. But such approaches may also be applied with a purpose to make the type of changes that are possible already through established approaches (such as genetic modification) more effective and easy to control (Hewett et al., 2016; Smansky et al., 2016). Ideas in this area are still on the theoretical drawing board or in very early experimental stages, albeit some accomplishments in recent years to create entirely synthetic chromosomes and organisms have received a lot of attention (Callaway 2014; Sample 2017). This area offers a higher level of granularity than gene editing, as it may involve nano-scale manipulation of the chemical building blocks of the components making up the DNA molecule (see further below about bionanotechnology), and therefore both maintaining and decreasing (in the dimensions of engineering ability and of effective barrier construction) the capacity for controlling how much the outcomes of applications interact with complex natural systems compared to gene editing, in turn affecting how widespread, longstanding and reversible the effects of such applications may be. As this field is still in an early stage, understanding of the basic mechanisms is still limited, albeit quickly evolving, while the holistic understanding is a recognised challenge, understood to bring severe problems of an ethical and regulatory nature as soon as the step is taken from basic research to innovation (Macnaghten et al., 2016). In addition,

synthetic biology has been claimed to present unprecedented risks related to military and terrorist applications (Ahteensuu 2017).

2.3.4 Bionanotechnology

So-called bionanotechnology refers to interventions that are undertaken at the molecular or even more granular levels, and has recently been increasingly highlighted as a potentially very potent family of technological approaches, e.g. in farming (Mukhopadhyay 2014; Parisi et al., 2015). Such approaches may include genetic modification, gene editing and synthetic biological applications, but combine it with other interventions targeting the basic chemical and physical structure of (natural or synthetic) organisms, as well as of components in (or to be added into) their surrounding environment, such as soil, water or air. Similarly it may be applied in industrial production whenever it involves some biological element, such as the use of organisms to produce compounds. What the bionano-approach potentially facilitates is a more finely controlled manipulated arrangement of both the organic and the inorganic aspects of an organism and its habitat. In its most advanced forms (at this time mostly on the drawing board or existing only in very experimental laboratory settings) it allows controlled re-arrangement of atomic or sub-atomic structures, and the constructions of new materials with specific features, as well as "machines" or "robots" that may be active within organisms to effect precise functional effects. For this reason, bionanotechnological applications offer the most granular type of biotechnology to date. While this facilitates opportunities to try to control and isolate the immediate effects of such applications from complex natural systems, it is also of a magnitude that increases the difficulty in this respect compared to genetic modification and gene editing. Therefore, reversibility appears to be less readily achievable, as the probability of products coming into contact with complex natural systems is raised. Once such contact is established, the potential for widespread and long-standing effects is very strong. The level of understanding in this area is at the same time recognised within the field to be limited at this point in time, and *holistic* understanding of how bionanotechnological applications would interact within complex natural and human social systems is seriously wanting.

2.4 Domains of risk, uncertainty and ignorance in non-human biotechnology

The mapping of the different types of biotechnology onto the typology of precautionary relevant features of biotechnology are graphically illustrated in figure 1.

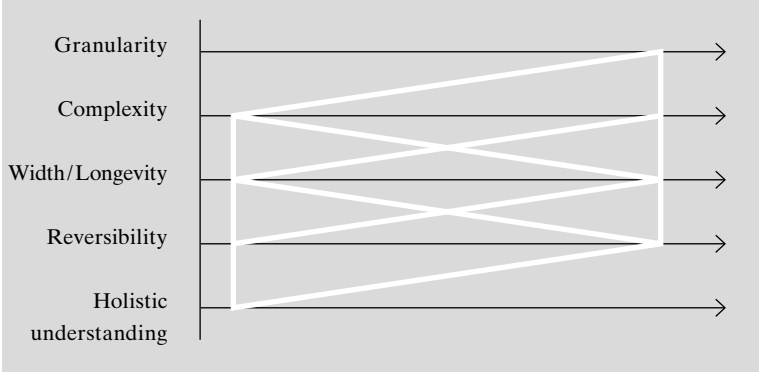

Figure 1: Synthetic biology/Bionanotechnology

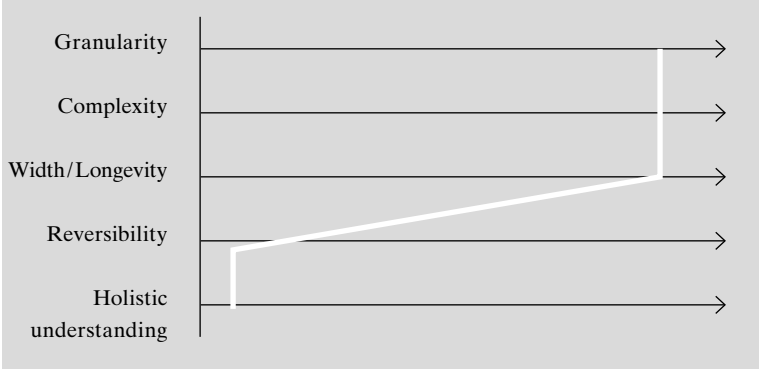

Figure 1: Gene driving

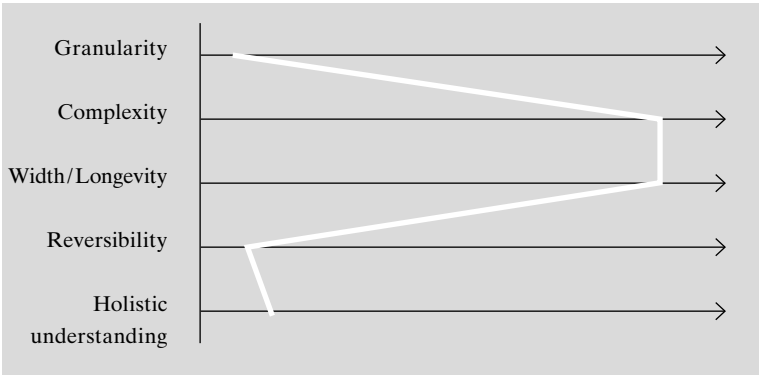

Figure 1: Manipulation macro structure / Moving, recreating and eradicating types

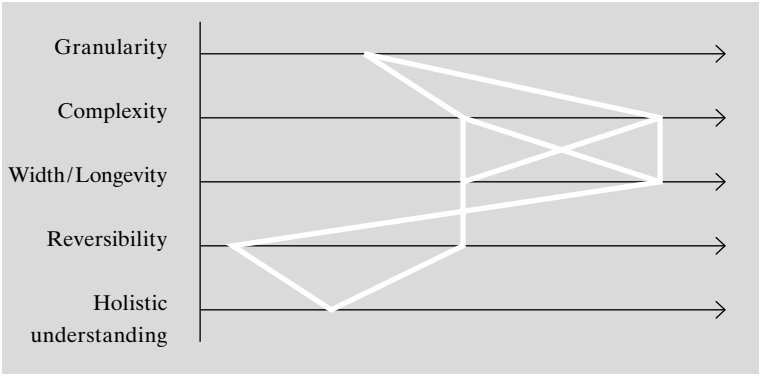

Figure 1: Breeding and crossing / Artificial mutation production

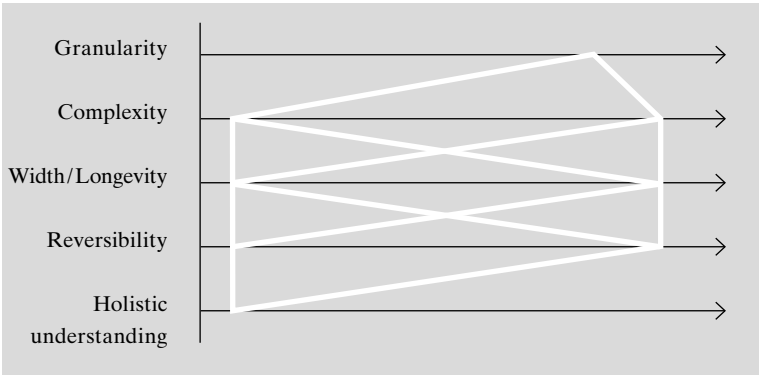

Figure 1: Genome editing/Genetic modification

Some noteworthy aspects of these patterns are:

- Ignorance in terms of *holistic* understanding of the overall (potential) effects is a general feature of all types of biotechnology. This is due to our incomplete understanding of longstanding and widespread interactions within and between complex natural and human social systems. Unreflected impressions of better holistic understanding of more established and traditional biotechnologies seem mostly to be based in different kinds of irrational bias, coming out of the fact that we are used to these technologies, that humanity had few alternatives to them when they were introduced (unlike now), making us more prone to accept downsides that can now be more readily avoided, believe their demonstrated bad effects to be safely in the past, and ignore that even very small changes may make currently apparently well-functioning solutions have devastating outcomes in complex systems.
- The most traditional biotechnologies (that are not very granular) are *more* likely to cause irreversible, widespread and longstanding effects in complex natural systems against a background of serious lack of holistic understanding than more granular technologies of later dates. This since the latter often allow control through better mechanistic knowledge and possibilities of applying physical barriers that may isolate outcomes from complex natural systems. In spite of this, these more recent technologies

are often more in the focus of critical debates, and special regulatory hurdles.

- High granularity of a biotechnology brings with it two aspects that possibly makes many people spontaneously view them as particularly risky/uncertain/dangerous: (a) the potential for effects to affect more types of physical systems, thereby becoming more widespread; (b) the increased difficulty and cost of constructing and managing effective physical barriers to isolate them from surrounding complex natural systems, (c) the necessary aspect of heredity, whereby effected changes of organisms (or other systems incorporating self-replicating mechanisms) are passed on and spread through reproductive patterns.
- Low granularity at the same time usually makes barrier solutions impossible, as the technology by its very nature has to involve direct interaction with complex natural systems. As these technologies are applied in a wholesale or macro manner (soil management, fertilisation and pesticide solutions, landscape modification and breeding and crossing are used throughout a large segment of farming etc., mining enterprises exploit entire landscapes in several places where similar materials are to be extracted), they moreover usually produce widespread changes across a great number of dimensions and sub-systems, organic as well as inorganic,
- At the same time: the *actual* risks, uncertainties and background ignorance of a specific biotechnological application of any of the types will always depend on its exact purpose and range. Except for gene driving, the more granular types of technologies offer the opportunity for application in research that can be maintained reasonably isolated from complex natural systems, although very high granularity may also undermine the effectiveness of such barrier solutions.
- In light of all of this, from a precautionary standpoint, many (if not all) existing policies and regulatory systems seem to make irrelevant distinctions between different types of biotechnologies. When it comes to regulation, *new* biotechnologies are only marginally of more concern from a precautionary standpoint than well-established traditional ones.

None of this implies that current regulations around, e. g. the use of toxic compounds in farming, or the special regulation of GMOs, should be abandoned. Rather, what is demonstrated is that whatever regulatory hurdles and processes are put into place, they should apply on equal terms to all types of biotechnology. This since the interest of regulating biotechnology from a precautionary standpoint is not based in the classification of such technologies, or if they are new or old, but in their characteristics with regard to granularity, complexity, width and longevity, irreversibility and holistic understanding.

This provides a basic and strong reason in favour of what has sometimes been called "technology neutral" regulatory solutions in a variety of areas, such as internet and computer technology regulation (Hildebrandt & Tielemans 2013): It is not the historical past or the taxonomic type of a technology that should guide the rules for using it, but its potential for doing good in a responsible way. This may, of course, be perfectly compatible with having specific rules or regulatory solutions that in specific contexts or limited phases focus especially on particular technologies or applications of these, in spite of what some critics of technology neutral regulation seem to assume (see, e. g. Azar & Sandén 2011). The important thing is that any such special solution must be supported by underlying, sound precautionary reasons, and therefore may lose its justification over time and for that reason need to be regularly revisited. This moves the question to what such sound precautionary reasons are and what may make them so.

3. The Precautionary Principle and the Price of Precaution

As mentioned in section 1.3, whenever "the" or "a" precautionary principle (PP) is mentioned, there is much debate on what it is. The history, sources and basic content of PP often point to two basic thoughts, both of which are political norms thought to ground basic legal obligations of states to form policy (Trouwborst 2009): one saying that it may be justified to take political action in order to avoid dangers also in lack of scientific proof, and another saying that such actions are in fact justified in case (and only in case) certain conditions are fulfilled (Gardiner 2006; Manson 2002; Munthe 2015, 2016; Sandin 1999, 2004; Steel 2014). The *ethics* of precaution regards what these conditions are and how they may be grounded in an underlying ethics of risk and precaution. Therefore and as mentioned in section 1.3 this section will be mostly discussing this latter issue, returning to what this means for a usable precautionary policy in the final subsection. I also remind about the concentration on the ethics of entire regulatory systems discussed in section 1.5.

3.1 The basic issue of the price of precaution

The area of the ethics of risk and precaution proceed from two basic assumptions that correspond to the questions mentioned in section 1.4:

- We have an ethical reason to avoid exposing people to risks, unless this is necessary in order to have sufficiently important benefits.
- When exposing others to risk is an unavoidable possibility, we should base our decisions on what risks to expose others to on sufficiently good information about risks and benefits.

Failing to act on the first tenet is a sort of ethical irresponsibility that can be compared to legal recklessness. The second can likewise be compared to a legally recognised form of irresponsibility, but in that case negligence. Avoiding irresponsibly reckless behaviour can be achieved by either abstaining altogether from an activity, or by applying precautionary measures that mitigate

the risk-benefit profile to make it morally acceptable. Avoiding irresponsibly negligent behaviour can be achieved by either postponing the decision on whether or not to start some activity, or by improving the basis of information that would make it possible to make a responsible decision.

This rudimentary part of the ethics of risk and precaution confirms a basic idea expressed by PP, namely that it has a moral price to act (overly) incautiously. Unless there are sufficient countervailing moral reasons, we should avoid such behaviour. However, it also clarifies a challenge in explaining what a precautionary stance requires from us, as proceeding cautiously will unavoidably bring its own downsides:

- Whatever measures are taken to mitigate possible risks or collect better information will require resources (including time) that could instead have been spent on securing more certain benefits.
- Whatever these measures are, they may also bring their own risks and immediate downsides, for instance risks or certain harm to animal or vegetable research subjects.
- While we contemplate whether or not some action is too risky, or while we collect more information to make a responsible decision on this action, we abstain from the possible benefits that this action would bring.

These three types of downsides form what I have called *the price of precaution* (Munthe 2011, ch. 1). The fact that acting to effect precaution has such a price means that there is an ethical problem built into the very idea of PP. This problem can be described in the form of the question: how high should the price of precaution be allowed to be? The point of turning to underlying ideas in the ethics of risk and precaution is to be able to provide an answer to that question, or at least to how that question could be answered in particular circumstances.

To illustrate the nature of this problem, consider this example using a biotechnological case (discussed in Munthe 2011, pp. 52–53, 120–122, 153–161):

… imagine a situation where we contemplate the use of genetically modified crop in order to reduce the serious environmental problems created by modern farming. This crop would not need the toxins and artificial fertilisers used with contemporary types of crop in order to produce a sufficiently rich harvest. However, scenarios can be described where the introduction of the new crop would in the future alter the ecosystem to such an extent that humans and many sentient animals would suffer very serious harm, and these scenarios are, we assume, sufficiently probable according to current scientific expertise […]

… precaution tells us that we should not use the new crop until it has been shown not to bring too serious risks. […] But, of course, the more time being spent on this, the more time will also be allowed for the currently on-going destruction of the environment caused by contemporary farming methods. And, since it will always be possible to expand and refine the evidence a bit further, there is in principle no end to the time that the requirement of precaution in this manner may prescribe environmental degradation to continue.

However, interpreting the requirement [of precaution] so strongly would, I take it, be seen by most people as moral lunacy. The protection against possible unwelcome future effects of the new crop provided by such a strong version of the requirement of precaution is simply not worth the price we have to pay in actual damage and harm. […] However, at the same time, just starting to use the new crop on a large scale without taking any precautions whatsoever against future disaster would, most of us would judge, be just as preposterous. That is, in that case, the prescribed degree of precaution would be unacceptably low.

This simplified example illustrates an issue that, for instance, seems to be of the highest importance for the on-going debate with regard to political action in the face of climate change. Whatever measures are taken to prevent undesirable effects of this phenomenon, these will impose certain costs in terms of money, quality of life and possibly also life. At the same time, scenarios regarding the actual preventive effects of these actions have to be uncertain (partly since the basic climate change scenarios are uncertain). For this reason, we find opinions on both sides with regard to whether or not the price of different suggested precautionary measures is in fact too high (or too low, for that matter).

So, where, then, do we draw the line? How much of actual environmental damage should we accept in order to investigate the possibility of future disaster being the effect of our putting a halt to our current damaging practice? More simple: what price in terms of certain present harm or value-loss are we permitted or obliged to pay in order to increase our security against possible future harm? Any more precise version of [an ethics] of precaution will need the support of arguments to the effect that its answer to the just posed query is morally acceptable. (Munthe 2011, pp. 52–53).

What we need from an ethics of risk and precaution is, in other words, concepts and reasons that may help providing more precise answer to this underlying conundrum in a way that may be useful for guiding actual policy on a more variable collection of biotechnologies.

3.2 Elementary requirements for a sound ethics of risk and precaution

Debates on the PP and its underlying philosophy, as well as on the ethics of risk, have produced a number of different proposals, many of which are incompatible or in competition with each other, and when philosophers and ethicists discuss the issue these are often in the main focus. In the following I will instead start by summarising what I have understood to be an emerging methodological consensus on a number of topical areas. This consensus does not set out any particular precise idea of what the price of precaution should (be allowed to) be, but rather presents conditions for what an acceptable answer to that question must live up to. After having briefly presented these, I will proceed to more contested underlying ethical issues, and demonstrate how some of these are effected by the methodological consensus. But also demonstrating how some critical ethical issues are still left open.

3.2.1 Non-arbitrariness and principled reasons

One condition which has come to shape a number of discussions about the possibility of understanding and justifying PP – assumed by all the contributors mentioned in the introductory paragraph

to this section, plus several critics (Munthe 2011, ch. 2) – is that whatever price of precaution is required by a version of PP, it must not be arbitrary. This is a general requirement on valid ethical arguments that they are based on consistent, principled reasons that apply equally to all relevantly similar acting parties and situations of choice. For instance, if I am to argue in a justified way that a particular biotechnology is morally irresponsible due to its overall dangers or uncertainties, I must be able to present an idea of what makes for irresponsible lack of precaution due to dangerousness that is *generally* valid not only for this technology, but for all sufficiently similar ones (in terms of potential dangerousness). That is, if that degree of dangerousness is to prove that the price of precaution of not using or postponing the use of the technology in question is acceptable, then it must have the same argumentative upshot with regard to all other biotechnologies to which it applies. If that is not the case, the argument rests on an arbitrary assumption and is invalid.

This requirement can be traced back to very basic tenets of moral philosophy that demand of ethical principles that they treat equal cases and affected parties equally, sometimes referred to in terms of human dignity or respect for persons, sometimes in terms of formal equality or practical consistency or rationality. The requirement of non-arbitrariness and access to principled reasons also fits very well with basic qualities that we tend to require of political and legal institutions. Such requirements are expressed, e. g. by principles of rule of law and equality before the law, and on bans on arbitrary arrest or other legal action in the UN declaration and European convention of human rights (Council of Europe 1950; United Nations 1948).

I will here provide three concrete examples of common precautionary arguments often heard in debates about biotechnological applications, which illustrate the function of requiring non-arbitrary, principled reasons. One example is when proponents of a technological application argue that it should not be impeded by precautionary regulation because of its (potentially large) benefits.[1] Such arguments seem to assume the principle that if an action

[1] Arguments of this kind have recently been advanced, e. g. in debates around research ethical regulation (Wilson & Hunter 2010).

seems to bring (large) benefits, then it should not be impeded. Such a principle would have as a result that more or less all kinds of safety regulation in all areas should be disbanded, for instance, regulation for the introduction of toxic chemicals in the working environment, or of new pharmaceuticals. Unless this consequence is acceptable, the argument cannot be sound and valid with regard to the biotechnological application in question. A second example is the opposite phenomenon, when an opponent of a biotechnological application argues that it should not be allowed due to uncertainties and risks of a sort that is accepted in other instances of biotechnological application, or in other areas of human technology use. This is rather common in the area of arguments against (traditional) genetic modification, as all or almost all of the risks and uncertainties seem to be about possibilities of widespread and longstanding irreversible effects in complex natural systems regarding which we suffer a lack of holistic understanding *that are shared with more traditional biotechnological applications* which are nevertheless accepted. A third example is when other arguments than those referring to risks of harm are considered, for instance, the often repeated "social argument" against allowing GMOs where the user of the product is dependent on the continuous provision by a particular commercial producer. As this is the fact in many areas of human consumption, for instance, with regard to pharmaceuticals, this argument must then apply equally to those areas, or be judged as arbitrary and invalid. None of this, of course, decides the issue of whether or not these applications should be allowed or regulated and, if so, how, but it constrains what arguments can be valid when debating such issues.

3.2.2 Non-paradoxicality

This idea connects to the former one, as it has been a very common criticism of PP, as well as arguments in terms of it or the concept of precaution, that these become paradoxical once they are formulated as principled reasons (Munthe 2013). There are a number of variants of such paradox, of which precautionary arguments and PP have been accused. One is about producing guidance that is impossible to act on (Munthe 2011), while the other is about producing inconsistent guidance (Steel 2014).

The first form of paradox is illustrated by the examples of a principle saying that if an action may pose some major danger, then it should not be undertaken, or one saying that if we lack absolutely certain knowledge that an action does not bring some particular danger, then it should not be undertaken. As all actions (including continuing doing whatever one is doing at the moment) *may* pose some major danger (albeit in many cases one that has not been actualised yet), and as human beings due to the very condition of our existence can never attain absolutely certain knowledge about any empirical matter, both these principled reasons would ban us from doing anything of what we can do (including what we are currently doing). This kind of paradox thus undermines the ability of such reasons to provide any sort of ethical guidance. The second form of paradox is illustrated, e. g. by the argument that a certain action should be avoided because it is dangerous, wielded in a situation where also the abstaining from this same action is dangerous. Again, the outcome is paradoxical and lacks ability to guide action, as we seem to be recommended to both do and not do the same action.

The paradoxicality is often a result of arguments or principles being badly formulated, or without recognition of the basic requirement on non-arbitrariness. However, while some critics have suggested that PP or precautionary reason *cannot* be more carefully formulated to avoid paradox (Harris & Holm 2002; Häyri 2005; McKinney & Hill 2000; Peterson 2006; Sunstein 2005), more recent analysis has pointed out a wide range of ways in which this is possible (Munthe 2011, 2013; Sandin 2004, 2006; Steel 2014). Nevertheless, there is consensus about the requirement that good precautionary reasons must not be paradoxical (Munthe 2016). The remaining ideas of this subsection describe a number of dimensions in which the ethics of risk and precaution need to provide specific clarification to satisfy that requirement.

3.2.3 Proportionality

The perhaps most obvious consequence of the requirements of avoiding arbitrariness and paradox is that a sound ethics of risk and precaution cannot support the idea that the mere presence of a risk, uncertainty or knowledge gap by itself settles the question

of whether or not a risky action, or a decision with uncertain consequences, based on partial ignorance, is responsible or not. The same, of course, holds for the presence of possible benefits and particular evidence. An acceptable price of precaution cannot be infinitely large just because of one sort of factor being present in a situation of choice, or because of the applicability of one reason against taking some risk or proceeding despite uncertain knowledge. Likewise, no possible benefit or piece of knowledge closing or narrowing a knowledge gap can completely undermine the notion of an acceptable price of precaution. An acceptable theory of the ethics of risk and precaution must allow for complexity, nuance and context.

An important upshot of this is that the assessment of what precautionary reasons there are for or against a particular biotechnological application has to consider both chances of benefits and risks of harms, as well as knowledge gaps with regard to both. A further reason in support of this conclusion is the observation that abstaining from harming or continuing a harmful activity can be seen as a benefit, while abstaining from benefitting someone or continuing to withhold a benefit can be seen as harming. Just as our reason to exercise precaution in the face of potentially dangerous or uncertain activities is mirrored by our reason not to allow the price of such precaution to rise too high, our moral reasons to abstain from harmful activities are constrained by similar reasons not to extend harm through the ways in which we did the former. An important consequence of this is that the question of which risks and uncertainties may be ethically acceptable is always relative to what other risks and uncertainties are at stake in a situation of choice, as well as to what chances of benefits are possible to realise through available options. The acceptable price of precaution of abstaining from or postponing some risky action, or action where we face serious knowledge gaps regarding its riskiness, may therefore vary considerable depending on what options are available. It may also vary over time, as available knowledge changes, or new options appear. The same holds with regard to single risk- or benefit-scenarios that may be linked to different technological actions (e. g. hereditary effects of breeding and crossing, artificial mutation production, traditional genetic modification and gene editing). Of course, this regards the reasons against as well as for the

suggestion that some technological application should be stopped or postponed due to precautionary reasons.

While there remain some details of possible disagreements (see below), the emerging consensus on a requirement of proportionality have some general consequences worth noting:

- Any justified precautionary action needs to be based in an ethical principle that recognises the need for proportional reasons for what price of precaution is acceptable.
- If an activity poses a risk, or a knowledge gap with regard to possible risks, this activity can be justified in terms of precaution only if this activity also presents a sufficiently substantial chance of benefit.
- If a precautionary action is justified, it should always be implemented in a way that minimises the price of precaution (given that the justified level of caution remains constant).
- New knowledge or new options (e. g. to mitigate risk scenarios of different applications) may always change the price of precaution with regard to a particular action.

Recently, reasons such as these have led to calls *in terms of precaution* for abolishing the kind of technology-specific regulation of GMOs that in many jurisdictions was put into place in the 1980's and -90's, when much less was known about these technologies and their existing options than today (Hansson 2016). *What* exact proportion of knowledge and knowledge gaps, risks and chances of benefits may support or oppose some precautionary measure regarding a specific biotechnological application, is always open for debate. However, if the reason for a higher price of precaution is lack of knowledge or ability to control risks, this reason may weaken as new knowledge and tools of control appear. Likewise, technologies that have been judged as acceptable may be seen in a more unfavourable precautionary light with time, as new alternative options appear and knowledge about effects on complex natural systems of the old technology become better understood. This regards, not least, if the new technologies offer hitherto unavailable opportunities for barrier solutions that may serve to mitigate risks and uncertainties coming out of the interaction with complex natural systems. This type of generalisation of Hansson's

line of reasoning also seems to be supported by Steel's conception of how the epistemic elements of precautionary regulation should be devised (Steel 2014, ch. 8–9)

3.2.4 Conservatism and "technology optimism"

Another consequence of the requirements of non-arbitrariness and non-paradoxicality regards how a defensible ethics of risk and precaution should relate itself to new and old risks and uncertainties. Precautionary and risk ethical reasons regard only two types of factors as relevant: information about dangers and possible benefits of options, and the quality of such information available in a situation of choice. Low quality of information may itself be a reason for precaution in the form of delaying some activity while collecting better information, as long as the price of this precautionary action is acceptable. Lack of proportion between risks and possible benefits may likewise be a reason for precaution in terms of abstaining entirely from an activity, as long as there is some option that presents a more responsible course of action. Whether or not a considered activity and its various options are "new" or "old" is of no consequence – regardless if the words mean "novel" and "established", or "familiar" and "unfamiliar". Nevertheless, a lot of precautionary regulation, not only regarding biotechnology in the non-human domain, focus exclusively on *new* applications, a sort of biotechnology conservatism. As a mirror image, in many areas where such specific regulation is not in place, there is often a considerable bias in favour of novelties, sometimes referred to as "technology optimism".

This aspect of precautionary policy and regulation has been a source of much criticism (Harris & Holm 2002; Sunstein 2005), and has been constructively addressed to some extent (Munthe 2011, ch. 2 and 6, Sandin 2004; Steel 2014). There is room to argue that the time of use of and familiarity with a technology may have an *indirect* impact on factors of more immediate ethical concern. For instance, time may allow systematic documentation of outcomes of actual use, improved understanding of mechanisms and holistic aspects through careful study of *in vivo* applications, and so on. At the same time, however, there are also the cognitive, emotional and intellectual biases mentioned in section 2.4, which

tend to have us overestimate our knowledge about and the safety of technological solutions we have grown accustomed to. It is easy to forget, for instance, that we who are here now in affluent circumstances, reaping the fruits of modern agriculture and biological processing industry, are so as a positively selected result out of a long history of development that has included many negative outcomes and resulting adaptations of both technological applications, institutional organisation and the way that human beings relate to these. Even small changes in our environment, such as minor variations of weather or political stability, may quickly change the prerequisites of our current technological solutions to function well. These solutions may also continuously be amassing gradual negative factors that eventually will pass physical thresholds to effect massive damage, albeit we are currently in no position to foresee this. In addition, our strive to develop new biotechnological solutions for, e. g. food and drug production, of course, depends on various downsides that we do perceive with more familiar methods currently in use, if nothing else in terms of production cost.

3.2.5 Opportunity costs and optional comparison

A final outcome of the basic requirements on a sound ethics of risk and precaution is that it supports the notion that *single actions can never be assessed from a precautionary standpoint by themselves*. They always need to be assessed in comparison to other alternative options, which are analysed in light of the other requirements mentioned. Even if there is a regulatory standard applied, against which proposed applications are assessed, this standard must include the possibility of assessing what an economist would call the opportunity costs of both allowing and (in some way) regulating this application. In case of the latter, these opportunity costs equal the price of precaution of that measure, i. e. direct costs for precautionary actions (such as research to clarify risks, or applied barrier solutions to mitigate risks), risks induced by such actions, and harm due to delayed or decreased possible benefits of the application this being regulated, e. g. by allowing risky and harmful "old" activities to continue. Thus, part of this cost is about the effects of alternative options that are being performed instead of the regulated application.

This makes the assessment of to what extent an application may be compatible with a sound precautionary policy more complicated than what is acknowledged in many contemporary systems for regulating biotechnology in the non-human domain. These usually apply a model of risk assessment and management that apply more or less pre-set "safety levels", typically used in a way that ignores the safety of existing and on-going practices and scenarios. This ignores the dynamic and complexity of the ethics of risk and precaution created the requirement to perform an optional comparison that includes an analysis of the opportunity costs of proposed precautionary actions (as well as suggested technological applications). This departure from a sound ethics of risk and precaution is not least evident in systems where the very fact that something is a GMO by itself discharges harsher regulatory monitoring and assessment, than if the application is classified in some other way.

3.3 Remaining ethical issues

This chapter is concluded by describing some remaining (rather wide) room for disagreement on the ethics of risk and precaution. The disagreements fall, roughly, into two different categories: either they are about the actual acceptable price of precaution of an ethically justified regulatory policy, or they are about how such a price should be accomplished, provided that we agree on it.

3.3.1 Entry thresholds for a precautionary regulatory system

One of the most debated issues in the ethics of risk and precaution, and PP, that remains open is how initially dangerous or uncertain a technological application needs to be in order for regulatory mechanisms to apply to it. This question is critical for what price of precaution will be required by a regulatory system, and there exists a large number of ideas about how to answer it (Munthe 2013, 2016, Steel 2014). A popular notion is the idea of *de minimis* (or negligible) risk: that very unlikely harms need not actualise closer scrutiny or regulatory action. But this suggestion is rivalled by the contrary notion that it is the size or the gravity of the possible harm that should decide if a technology should be more closely scrutinised or tightly controlled. A third suggestion is that a sensible

solution to this issue needs to consider a combination of these factors, allowing for regulatory action due to very serious though unlikely hazards (as in the case of regulation around nuclear power plants and facilities for storing high grade nuclear fuel), but also that activities which are very likely to cause harm, albeit very minor one, may escape further regulatory attention. In addition, there is the problem of knowledge gaps, and the fact that human imagination may produce a lot of catastrophe scenarios, as well as miss very credible catastrophe scenarios, depending on how much we have studied the matter. This is the idea underlying standard regulation of the introduction of pharmaceuticals that requires of all such technological applications that whatever claims to benefits and risks they make are backed up by scientific research.

In all of these dimensions, the lower the bar is set for whatever regulatory requirements are applicable, the more technologies and applications will be the subject of regulatory action, and the higher the price of precaution will be paid by such a system. Likewise, the higher this bar is set, the fewer technologies and applications will be the subject of regulatory action, and the lower the price of precaution will be paid by such a system. This holds regardless of what principles for assessing knowledge gaps, risks and uncertainties are then applied within the regulatory system. Plausibly, the entry threshold should be set somewhere in between extremely high and extremely low prices of precaution. But it is difficult to specify more than this without entering into controversy.

Steel (2014) has recently addressed this issue in epistemic terms, and held out that it is consistent with basic tenets of science and risk analysis to require that "unproven" dangers as well as lack of general qualitative evidence may suffice for passing the entry threshold. At the same time, the basic requirements on a valid ethics of risk and precaution imply that there also has to be a limit somewhere, lest the system will become either arbitrary or paradoxical. The question of where that limit should be also actualises the requirement of proportionality, especially the issue to what extent the *possible benefits* of a technology of an application should have an impact of where its entry threshold is set. One ethical theory of the ethics of risk and precaution suggests that it should, but that this idea actualises further problems (Munthe 2011, ch. 5). These will be somewhat addressed in the subsections to follow.

3.3.2 Rigid and variable normative structures within a precautionary regulatory system

A remaining question is to what extent a valid ethics of risk and precaution may be consistent with absolute or rigid ethical bans against certain technologies or technological applications. Munthe (2011, ch. 2, 4, 5) has discussed this issue at length with somewhat sceptical results. The requirements of non-arbitrariness, non-paradoxicality and proportionality combined seem to imply that ideas like the one famously suggested by Hans Jonas (1979) of viewing *particular outcomes* as absolutely forbidden to risk – no matter the context, likelihoods or knowledge gaps – are impossible to justify. This since risks of some magnitude or uncertainty of whatever outcome is considered for such an absolute ban[2] will always be present, no matter what option is considered. In fact, this difficulty is one of the main reasons for the need for proportionality of a sound ethics of risk and precaution: as risks and uncertainties are different from actions in that *total avoidance* of them cannot be guaranteed by the choice of options, ethical principles need to focus on some idea about *feasible* avoidance, which will be cashed out in terms of requirements to go for less serious rather than more serious risks or uncertainties – not of avoiding risks and uncertainties altogether (as that is impossible).

This limitation need not completely undermine the notion of more rigid risk ethical principles, as long as these are defensible in other ways. For instance, it may be possible to build into the conception of proportionality more sophisticated deontological ideas that restrict not the risking of set outcomes, but how the balancing of risks and benefits are aggregated. One idea, for example, may be to consider limits to how risks of harm and chances of benefits to individuals are balanced against aggregated collective harms and benefits, so that some idea about non-instrumentality in the spirit of the Kantian dictum that a person must never be treated merely as a means to the ends of others is preserved within a risk ethical framework. At the same time, the risk ethical context presents more of a challenge for the consistent formulation of such ideas than the ordinary ethical setting, as the most ethically serious risks

[2] Jonas' own famous example is the outcome of having humanity exterminated.

and uncertainties are typically produced collectively by incremental individual contributions (most environmental risks are of this sort). From this standpoint, ethically justifiable precaution is often more of a public than an individual good, and an ethics of risk therefore needs to contain elements to secure it. Political action to this effect will therefore almost always mean acting towards *some* particular individuals with greater force than what is justified in a typical deontological conception of justifiable action to prevent wrongdoing (as no individual is creating the ethically unacceptable risk or uncertainty). It has not been proven impossible to achieve such solutions, but it has been noted that typical deontological ethical theories are less developed than typical consequentialist ones in this respect, albeit very recent work has demonstrated that deontological formulas may be made quite sophisticated (Kamm 2006). It remains to be seen if such developments can be extended to satisfy the needs and requirements of a sound ethics of risk and precaution (Munthe 2011, ch. 5).

Now, these more fundamental challenges for ethical theory are at the same time consistent with having justified rigid solutions at work within a precautionary regulatory solution. An obvious example of this is the choice of principles for the entry threshold (see the preceding subsection). Such a threshold can be designed so that regulatory action is triggered as soon as a technology or application may theoretically actualise specific types of risk-levels or -scenarios (regardless of the context). This will not mean that they are automatically banned, but it implies that they must be subjected to further scrutiny and assessment from a precautionary standpoint before given the green light. For instance, this may be a reason to have *all* biotechnological applications that interact with complex natural systems (and thereby are prone to bring widespread and longstanding irreversible effects of which we have weak holistic understanding) pass the entry threshold for further precautionary regulative action. As noted earlier, it would not be consistent with the requirement of non-arbitrariness to apply such a principle only to a subset of such biotechnologies, for instance, only new ones.

While a rigid entry threshold can be defended ethically (provided that the effected price of precaution can), the principles applied to activities *within* the regulatory system must, however, be

flexible to the various factors that follow from the requirements of proportionality and of sensitivity to opportunity costs and optional comparison. If it is not, it risks violating the requirements of non-arbitrariness and/or non-paradoxicality. This will necessarily allow for rankings of various levels and types of knowledge gaps and risk and benefit scenarios in terms of worse and better, and some such gaps and scenarios may very well be ranked as very serious and difficult to justify from a precautionary standpoint. However, also in these latter cases it will remain possible to justify use of the technology in case the optional context and actual stakes are extraordinary. Here we may compare with an often discussed type of situation in medicine, where an acute and grim prognosis in combination with lack of effective treatments in an acute situation may sometimes justify the use of experimental procedures that could be very harmful and of which very little is known, and which would otherwise be completely out of the question.

This logic works also the other way: even if some technology or application is well confirmed to pose *minor* risks, these may not be worth taking if the chances of benefit of this technological application is too slim, or satisfactory alternative options are already available. As most biotechnologies and applications are risky and uncertain to some extent, it therefore makes sense to start with analysing what benefits they may bring (in comparison to alternative options). If these are too slim to justify even minor risk or action in the face of knowledge gaps, proceeding further to assessment of risks and uncertainties becomes unnecessary due to the basic tenets of the requirement of proportionality. Again, such assessment must, of course, observe the requirements of non-arbitrariness and non-paradoxicality – treating technologies and application that are similar in terms of risk-benefit profiles and knowledge gaps according to the same precautionary standards.

If sufficiently substantial chances of benefit instead do exist, it then remains to assess to what extent the technology or application in question should be allowed in view of its risks and knowledge gaps. As observed, when a technology is very new, it often makes good sense to require postponing application while conducting further investigation in order to narrow existing knowledge gaps. However, such delay cannot be justified to continue indefinitely: at some point the basis of knowledge will be of compatible quality

to other technologies that have been accepted for further assessment (regardless of if that has resulted in a ban or permission). As observed, such assessment of risks and chances of benefits may then differ considerably depending on the more exact application, and may result in conditional approval for use only under special restriction, such as the application of various barrier solutions to increase safety. Again, if they are to enjoy ethical support, all of these assessments need to be based on a precautionary standard that prescribes an acceptable price of precaution.

3.3.3 Balancing risks and uncertainties: knowledge gaps and the weight of evil

What, then, should this precautionary standard be? This is without doubt the most theoretically challenging of the ethical issues of risk and precaution that remain even if we agree on the basic requirements formulated in section 3.2. As mentioned, it needs to consider both of the basic dimensions of the ethics of risk: how knowledge gaps should be assessed ethically, and what balance of risks and possible benefits should be required for a technology to be assessed as ethically acceptable from a precautionary standpoint given some calculation of these risks and benefits.

The former issue presents particular difficulty, as it is impossible to solve in a non-arbitrary way within the frames of state-of-the-art risk analytical models (Munthe 2011, 2013, 2016). Simply put, these models all say something about how to assess risks and benefits given a suggested calculation of what these are. But, as mentioned in section 1.4, such a calculation may always be revised on the basis of further information, which undermines the confidence of whatever assessment we make based on our current basis of information. Should we, therefore, postpone our decision and update our information, or make our decision based on the information we have? This is a question that presents profound difficulties: Unless we know *either* that no such revision would make a difference to what would be ethically justified to do (which requires that we also know what ethical principle to apply when assessing the balance of risks and possible benefits), *or* what recommendation would come out of such a revised calculation of risks and possible benefits (which we cannot know, but in which case it would be unnecessary

to update the information), we seem to be given no clue on how to act, unless we can present further guiding principles. In decision theory and economics, suggestions for such additions have been made in terms of the concepts of *decision costs, epistemic risk* and *value of information* (Munthe 2011, 2016). These suggestions illustrate that *if* a defensible ethical principle for the problem of knowledge gaps can be presented, it may be fitted into the standard risk analytical apparatus. However, they do not themselves embody such a defensible principle, as by themselves they all violate the requirement of non-arbitrariness.

As a way forward, Munthe (2011) has suggested that whatever detailed solution to this problem is considered, it must rest on the ethical principle, that it is always ethically desirable to make decisions on a firmer basis of information. That is, there is always an ethical reason to narrow or close knowledge gaps before deciding on whether an action presents an ethically acceptable balance of risks and possible benefits. This reason, however, is not conclusive, but must be considered in the light of all other reasons available in a situation according to the general idea that no ethics of risk and precaution must prescribe an excessive price of precaution, and observing the basic requirements set out in section 3.2. Based on this sketched solution, the problem of knowledge gap is transformed from being a unique problem, into being one aspect of the problem of balancing risks and possible benefits of alternative options. It does so by adding to every situation of choice regarding whether or not to use a technology or particular technological application the option of postponing this use to search for better knowledge. Whether or not to opt for that solution will then have to be decided in the context of every situation of choice, the options it offers, the quality of the underlying information, and what is at stake in this situation. Typically, if this situation regards a new technology that replaces on-going practices which are known to be very bad, postponing the decision on whether or not to accept the risks and knowledge gaps regarding the technology will have high price of precaution, increasing in relation to how long the decision is delayed and how destructive the on-going practices are. In section 3.1, the example of a genetically modified plant that could significantly reduce a number of known environmentally destructive farming practices illustrated this point. An even better

illustration is the case of considering *research* using biotechnology for better understanding the mechanisms underlying the environmental damages and risks, as well as possibly developing new and better biotechnological solutions, using technological interventions of a granularity that allow for effective barrier protection against the risks and uncertainties that would result from interaction with highly complex natural systems. As mentioned, very high granularity can here pose a challenge, as it undermines the reliable effectiveness of barriers. However, in light of the fact that we do allow research in physics with a number of theoretically possible very serious risks and uncertainties, as long as this is done within ambitious protective shielding, it would seem difficult to argue even against bionanotechnological research, albeit it may make sense to require considerable safety arrangements.

This takes us to the last question of how an ethically acceptable balance of risks and possible benefits must look like. Part of the answer to this question is provided by the basic requirements in section 3.2, excluding both morally irresponsible lack of precaution as well as exaggerated or "extreme" precaution. But there remains a critical question: While participants in the debate agree on the principle that equally morally serious risks and chances of benefit cancel each other out (Munthe 2011, 2013, Steel 2014), it remains to be decided *what makes a risk and a chance of benefit more or less morally serious*. Munthe (2011, ch. 5) has concluded from the debate that part of the answer has to come from considering the magnitudes of likelihoods and harms/benefits according to a general idea of "calculated risk-taking" generally assumed in standard risk analysis. However, these magnitudes may be ethically assessed differently, and the calculus of the ethical status of an instance of risk-taking may therefore be designed in different ways. If moral seriousness is determined by these magnitudes alone, what we get is an ethical principle akin to the standard risk analytical notion, expressed in the basic models of risk-cost benefit analysis, and sometimes referred to as "risk neutrality" (Hansson 1999). However, there is also room for having more serious (possible) harms be a more important consideration than more serious (possible) benefits. This idea of an elevated "weight of evil" expresses the common idea that it is more morally serious to harm someone more than to fail to benefit someone more, even if the harm is on

a par with the benefit in terms of magnitude. In a similar vein, to justify risking more serious harm could be seen as requiring more than comparable chances of benefits. This opens up for a range of possible positions on "the weight of evil" that could all satisfy the basic requirements on a valid ethics of risk, illustrated in figure 2 (Munthe 2011, p. 102):

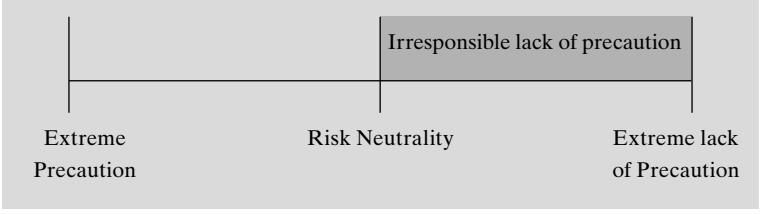

Figure 2

A minimally required ethical standard required for responsible precaution is thus to observe the "risk neutral" notion of defensible calculated risk taking. Already this may very well require substantially higher prices of precaution in many areas of societal technology policy than what is customary in current practices, due to a technology optimistic bias being dominant in most societies (Hansson 1999). If the weight of evil in an ethics of risk and precaution is increased, moving to the left from risk neutrality in the figure, the price of precaution will also increase, reflecting the idea that taking precautionary action such as delaying, disallowing or qualifying the use of some technology is worth more in terms of direct costs, new risks and opportunity costs of abstaining from the possible benefits of using the new technology. In terms of the former example of a new biotechnology that could help to reduce environmentally harmful farming practices, this move will mean accepting more of the damage resulting from allowing the current practices to continue. While such a price may seem to be hard to accept ethically already on moderate levels, other cases may present situations when increasing the price very much is easy to justify ethically, for instance, in the case of technologies or applications that bring very limited possible benefits (as when the application is just another variant of consumer product that allows a commercial company to hold onto a position in the market), or when

there are alternative options that present a reasonably satisfactory solution to whatever problem is addressed (such as providing food, producing pharmaceuticals, produce construction material, et cetera).

Arguments against the idea that risk neutrality is always sufficient for ethically responsible calculated risk-taking, and that a plausible ethical idea of precaution needs to move to the left in figure 2, point to basic ethical notions of outcomes having more of a moral significance than likelihoods, or simple mathematical combinations of outcomes and likelihoods. This can be demonstrated by considering a choice between two lotteries (these can be, for instance, two risky options), one in which I face the outcome of either winning €1 with a probability of 0.5 or losing €1 with a probability of 0.5, and one in which I face the chance of winning €10 000 with a probability of 0.5 or losing €10 000 with a probability of 0.5 (Munthe 2011, pp. 103–104). According to the idea of risk neutrality, and standard risk analytical models, these options are on a par (as their respective expected value are the same, namely zero), but most people would assess them as significantly different, due to the different magnitudes of the outcomes. The ethical aspect of this becomes clear as soon as the monetary values are exchanged for morally salient upshots, such as keeping or not keeping a minor promise to a friend versus murdering a friend or not murdering a friend. Clearly, avoiding having to risk murdering your friend is worth risking a minor lie. This indicates that a plausible ethics of risk and precaution should accommodate for higher prices of precaution than risk neutrality implies in at least some types of situations.

I will conclude this subsection by briefly describing a suggestion by myself as to *what*, more exactly, determines *how much and when* we are morally required to apply higher or lower prices of precaution. A more technical presentation of this idea that also addresses a number of potential problems can be found in my book *The Price of Precaution and the Ethics of Risk*, under the heading of "relative progressiveness" (Munthe 2011, pp. 118–129). The starting point for this idea is that the price of precaution of some technological action should be set in relation to a reference index, consisting of the presence or non-presence of alternative options that present decent or satisfactory solutions (in terms of chances

of benefits, risks and knowledge gaps) in a situation. As mentioned earlier whether or not there is such an option may change between different situations, and an option that is satisfactory in one context need not be it in another context (depending on what is offered by the available options there). If such an option is present, this will make the risks of other options in that situation more morally serious (or less worth taking) – *how much* more serious can be varied. This means that these other options have to offer more in terms of possible benefits (including the avoidance of existing risks) in order to be justified from a precautionary standpoint. It does *not* necessarily mean that the index option is the one that should be chosen, it may be that some of the other options are able to promise such upsides that the extra morally serious risks they bring are nevertheless responsible to take.

There are two ways in which a situation of choice may present this type of index option. One is if current practice offers a "good enough" solution to whatever problem that a technology offers a solution to. The other is if there are other alternative options, not yet implemented, that present such a "good enough" solution, for instance, a more cautious variant of the considered new technological application that applies more of safety barriers that mitigate extreme risk scenarios at the price of higher cost and/or lower chances of benefit, or a variant of already present solutions, modified to boost effect without too much of additional risk or uncertainty. This idea has one very important implication, namely that dire circumstances may justify less of precaution, as there is no "good enough" technological solution present. However, this holds only as long as we assume that no one else may provide safer solutions (and pay for them); if such options exist, the price of precaution goes up, but the duty to pay it is transferred to those better off. In contrast, in circumstances where the situation is, on the whole, quite good, taking further risks or accepting more uncertainties in order to gain some further benefits becomes less easy to justify: here the price of precaution can be allowed to become quite high. Many applications of biotechnology in the non-human domain contemplated for affluent settings – such as most European countries – seems to correspond to this latter situation. If we, among these, consider those applications that hold out only very minor chances of benefit (such as the benefit for a particular

company to hold on to market shares), the reasons for a high price of precaution increases even more. At the same time, research applications that could present solutions to important problems for people in dire circumstances, while more serious risks can be mitigated through barrier solutions, would seem to justify less of a price of precaution, even if the research is carried out in an affluent setting.[3]

3.4 Challenges in practical application: the pragmatics of policy

In section 2, a general conclusion was that, from a precautionary standpoint, regulation of biotechnology in the non-human domain should be "technology neutral". Rather than focusing on certain types of biotechnology (according to some taxonomy), it should focus on features of technologies and applications of immediate relevance for ethical assessment based on precautionary considerations. It was noted that, due to pragmatic considerations regarding easily interpreted and implemented regulation, particular types of biotechnology could be the object of "blank check" precautionary regulation during phases when they pose drastic knowledge gaps. However, the justification of such simplistic arrangements disappears as research clarifies how such a technology works. The major features of biotechnology in the non-human domain of concern from a precautionary standpoint are shared by all types of biotechnology, old as well as new ones. This initial conclusion has gained considerable support in the present section.

At the same time, this conclusion may create a challenge for the reality of the politics of environmental regulation. Many countries, not least across Europe, partly through European Union legislation, have adopted a similar type of regulation focused on GMOs. As mentioned at the outset of this report, this regulation is being quickly undermined by the use of gene editing for facilitating artificial mutation production with the same outcome in terms of the genetics of the resulting organism. That is, exactly the same types of fabricated organisms that today are regulated by special rules will soon not be so, without any notable change in terms

[3] This would be one of very many ways in which parts of the world that are better off may assist those less fortunate to improve their situation.

of what is relevant from a precautionary perspective. The latter organisms and the uses they are put to will be as precautionary motivated or unmotivated as their former GMO-siblings. Further into the future this process will be accelerated by the introduction of synthetic biotechnology and bionanotechnology. At the same time, the more important of the precautionary reasons that could be mustered on that matter also strongly suggest that these reasons are not really affected by *national* regulation. The major risks and uncertainties of precautionary importance to our assessment of biotechnologies are produced not by single countries or regions, but by the assembled global use of such technologies. The ethics of precaution of biotechnology in the non-human domain in this way is akin to many other environmental challenges: they require global solutions. However, global or multi-national regulative solutions are very difficult to engineer, if nothing else due to strong preferences for national sovereignty. Therefore, if multinational agreement on any type of regulation has been achieved, most parties would be reluctant to try to change it even for the better, as this means risking the multinational consensus altogether. Thus, given the case of technology *selective* multinational regulation being in place, there are pragmatic factors that work against an otherwise ethically well motivated change to a technology neutral regulative system. At the same time, to the extent that industry and research is now moving into making genetic changes with the use of gene editing, and (a bit further on) construct entirely novel life forms from scratch, and hybrids of living organisms and machines, neither of which will be seen as GMOs in the legal sense, moving to revise the old regulation makes increasing precautionary sense, even if that brings a risk of losing some international consensus.

On the other hand, it is rather clear that precautionary ethical reasons regarding biotechnology in the non-human domain favour political and regulative solutions on multi-national, preferably global, levels (Munthe 2011, ch. 6). Such aspects of precaution challenge existing political systems in a similar way that climate change does, and this aspect has begun to attract some attention in the academic ethical analysis of precaution (Hartzell-Nichols 2017; McKinnon 2011). A basic observation to make is that, from a global perspective, what each state does in terms of regulation

should ideally combine into a satisfactory global solution. In terms of precaution, this may mean (as observed earlier) that some states may ethically accept higher prices of precaution than others, allowing less affluent countries to take more risks and proceed in the face of more drastic knowledge gaps to improve their situation, than states in Europe and North America, for instance. However, we also saw that a conclusion may be that countries that are better off should take on some of these burdens, for instance by hosting the use of risky technologies that are important for developing countries to develop, or to simply sponsor better technological solutions abroad. The global aspect of the ethics of precaution may also mean, that precautionary policies that look satisfactory at a national level become unsatisfactory when they are added up at a global level, combining into either too excessive or too lax precautionary regulation altogether (Hansson 1997). If nothing else, therefore, it makes sense for a state to attempt to construct its precautionary regulation in international collaboration, and to be prepared to adjust it in light of how other states contribute and position themselves. Precautionary policy is, at heart, a cosmopolitan project that brings all of the challenges of cosmopolitan politics (Munthe 2011, pp. 22–23, 175–181).

The same phenomenon that creates part of the challenge of global precaution – the fact that many satisfactory parts may sum up to an unsatisfactory whole – reappears also with regard to domestic precautionary regulation. Here, instead, the problem appears when regulatory solutions are focused on looking only at risks and uncertainties of *single applications*, rather than significantly similar (from a precautionary ethical standpoint) families of applications (or technologies). This as many of the most serious knowledge gaps and risks with regard to biotechnologies in the non-human domain link to broad patterns of use of types of technological solutions – for instance, the risk of resistant weeds and other kind of unwanted evolutionary selective side-effects emanate from a long time of consistent use of a particular type of biotechnological application in a certain way. However, in our current regulatory systems (of GMOs), these risks and uncertainties are not being picked up at all, as the rules require only that each application is assessed on its own, and not in the context of a broader pattern of practice of which it is a part. At the same time, the

piece-by-piece assessment solution is the standard way of regulating introduction of risky technology – in a similar way, pharmaceutical licensing regulation does not pick up risks and uncertainties linked to the emission of pharmaceutical agents into the environment, e. g. antibiotics that drive antibiotic resistance development (Bengtsson-Palme 2016).

Observations such as these have led some commentators (Ahteensuu 2008; Hartzell-Nichols 2017; Munthe 2011; Sandin 2004) to suggest that the most basic ethical ideal with regard to precaution should not be seen as *a principle*, but rather an ethical criterion for entire policies, where different principles may be mixed with each other. Further doubts about the idea of PP as a formal decision-making tool (Munthe 2013; Peterson 2006) also supports the idea of precaution as a quality not primarily of single decisions, but of entire packages of policy solutions, within which regulation of decision-making may be one part.[4] A good precautionary policy for biotechnology in the non-human domain must express a proper price of precaution (supported by a sound ethics of risk and precaution that defines what determines such a price), but need not consist of one decision-making rule requiring this price to be paid in every single instance. On the contrary, a good precautionary policy should always focus on the overall effect in terms of the effected price of precaution, and must therefore be capable of discharging itself at such a general level. This may imply, for instance, that some extremely uncertain and potentially hazardous technologies (such as many synthetic biological and bionanotechnological applications) should be completely banned in almost all of its forms, although one may theoretically imagine particular applications that might be defensible, while others may have to pass only very cursory assessment, and yet others (the use of which may sum up to ethically unacceptable risk and uncertainty levels) are assessed on a case by case basis that is less allowing than a piece-by-piece assessment in terms of the price of precaution of a singular application would effect. The aim of policy, as mentioned in section 1.5, is usually not perfection in every single instance, but an acceptable result all things considered, where the

[4] Other parts of such a policy may include tax- and subsidy solutions, and other sorts of economic incentives.

overall upshot manages to err on the right side. In effect, rather different decision-making principles may very well apply to different proposed technological applications, albeit not in terms of the *type of technology*, but their respective risk and uncertainty profiles.

A final pragmatic challenge to be noted relates to the observation that the fact that a biotechnology or biotechnological application is new or old, or established or novel, seems to have almost no bearing whatsoever from a precautionary standpoint. In particular, it has much less bearing than what is apparently assumed in policies concentrating on precautionary screening only of *new* technological applications. At the same time, this is the typical form taken by precautionary technology policies; it may be noted that the commission to which this report is a delivery seems to presuppose exactly such a construction of "regulating *new* biotechnology in the non-human domain" as especially called for. However, sound ethical reasons strongly suggests that it is only marginally more important to assess novel biotechnologies than established ones (due to the often deep and wide knowledge gaps existing before a new technology has been tested thoroughly), and that we may assume for good reasons that our common sense of safety regarding established biotechnologies in the non-human domain is largely due to irrational bias. A sound ethics of precaution therefore suggests that, albeit a defensible precautionary policy regarding biotechnology in the non-human domain may include regulatory screening of new technological applications (according to the guidelines given earlier), this should not be the only ingredient. Just as we may have precautionary reason to resist or delay the introduction of a new technological application due to knowledge gaps and an unfavourable risk-benefit profile, we may have such reasons to abandon the use of established technological applications to the benefit of new ones, which have been shown to be more responsible in terms of risk and uncertainty. To the extent that this is precautionary motivated, regulating the new should include phasing out the old, thereby requiring new shapes of policies compared to existing regulatory systems. Anybody familiar with the realities of politics understands that such a regulatory policy will meet with much more resistance (from those who want to continue using the old technology) than one that only seeks to screen

novelties with which no one is yet familiar. For practical reasons, therefore, a working regulatory policy may have to accept some imbalance and pragmatically motivated conservatism in order to effect necessary support.

4. A Model for Assessing the Proper Price of Precaution Regarding New Biotechnologies

A main result of the former section is that a policy regarding biotechnology in the non-human domain that can be defended on the basis of a sound ethics of risk and precaution should not only be about regulating the introduction of new technological applications, should not only focus on the precautionary screening of individual biotechnological applications, and should not be restricted only to particular types of biotechnology, but be "technology neutral". It should also include assessment of old or established technologies, and the phasing out of these as new solutions make old ones morally irresponsible due to known risks and uncertainties. It should, moreover, complement a system for screening individual applications (new and old) with solutions that require assessment of the overall level and price of precaution produced by larger collections of applications. Finally, it should support precautionary measures proportionally to the risk-uncertainty profiles of technological applications, and nothing else than that.

These precautionary measures may take many different forms, but may be divided into a formula of what Daniel Steel has called "the tripod", consisting of "a knowledge condition, harm condition, and recommended precaution". The first two of these govern when some application qualifies for regulatory action, and the third indicates what the regulatory action is. My result in section 3 also agrees with Steel's notion of these as flexible and sensitive to contextual factors (2014, pp. 9–10). However, the analysis in this report (as well as Munthe 2011), *also* views the knowledge and harm conditions *not as distinct from, but as parts of* "a recommended precaution", e. g. a regulatory system for screening new technological applications that expresses a proper price of precaution. This is a direct upshot of the fact that the present analysis (in contrast to that of Steel) focuses on *ethical* aspects rather than scientific and epistemological ones (Munthe 2015). Thus, I here suggest that a defensible precautionary policy consists of a modified "tripod" consisting of what I above have called an *entry threshold* (including Steel's knowledge and harm conditions), an *ethical standard* for balancing the benefits, risks and uncertainties of technological applications overstepping the threshold, and an *arsenal of actions* to

discharge related to such applications depending on the outcome of applying the ethical standard. The entirety of such a construction should effect and express a defensible price of precaution, and must conform to the basic ethical requirements set out in section 3.2.

There are basically three variants of regulatory policy to consider:

1. *Pre-review of the knowledge gaps, risks and chances of benefits* posed by an application if an entry threshold is overstepped, with different further actions following depending on the outcome of the review.
2. *Moratoria (temporary limited simple bans)* for entire classes of technological applications that overstep an entry threshold.
3. *Simple bans* (unlimited) for entire classes of technological applications that overstep an entry threshold.
4. *Temporary limited simple permission* for entire classes of technological applications that do not overstep an entry threshold.
5. *Simple permission* (unlimited) for entire classes of technological applications that do not overstep an entry threshold.

In section 3, we saw that these variants may connect in various ways, and this can now be made clearer. For instance, if an application does not overstep the entry threshold for variant 1, it is likely to be subjected to either of variants 4 or 5. Moreover, review according to model 1, may lead to further actions 2 or 3, but also to milder regulatory measures, as well as no further measures at all, i. e., actions 4 or 5. In the following, I will comment especially on the variants 1–3.

4.1 Variant 1: Pre-review

This variant of a precautionary regulatory system can be described in terms of the "tripod" mentioned earlier: entry threshold, ethical standard and arsenal of action. Figure 3 at the end of this subsection provides a schematic overview of its components and possible variations.

The entry threshold is determined by the extent of ignorance and/or uncertainty regarding relevant fact related to potential risks and benefits, and the known existence of a risk-benefit profile

containing sufficiently likely or serious potential downsides. Applications that may escape such required review would thus be those where there is (a) very good knowledge about what risks and benefits may come out of using it, *and* (b) where these do not include any sufficiently likely or severe risk-scenarios. Based on the observations made earlier, this threshold should be set in conformity to the basic principles set out in section 3.2, and not only in terms of the risks and uncertainties of individual applications, but also by the expected mass of applications resulting from actual use that would follow a regulatory green light for the application in question (see section 1.5). As mentioned in section 3.1, this may allow rigid requirements for pre-review for entire classes of biotechnological applications, provided that it can be motivated in relevant terms. Such increased rigidity at this level will increase the price of precaution of the system, and must thus be justifiable in that light.

The review itself includes assessment of the actual knowledge gaps, risks and chances of benefits based on principles sketched in sections 3.2 and 3.3, and also here the expected outcome of systematic use should be included. The most important of the principles is that whatever balancing of benefits, risks and uncertainties determines the decided response out of the arsenal of actions, these must conform to the basic ethical requirements in section 3.2. On top of that, they may apply more or less elevated weights of evil as demonstrated in section 3.3, e. g. according to a model of "relative progressiveness". One critical stage in such a review is to determine the potential benefits of the application (related to alternative options available), as slim benefits combined with substantial uncertainties or risks (again related to alternative options) will usually make an application difficult to defend from a precautionary standpoint. Typical examples of slim benefits are those consisting of mere monetary gain for some individual party. Moreover, the outcome of the review has to be sensitive to factors that may change over time as well as between contexts, such as what knowledge is available and what alternative options are feasible. The more that feasible options are assessed as securing a "good enough" solution of whatever problem a technological application targets, the more difficult it becomes to justify that new risks or uncertainties are introduced to effect additional benefits. If, in contrast, there are

dire needs lacking solutions, this may justify increasingly substantial risks and uncertainties to effect better handling of these needs depending on their gravity and urgency.

The outcome of this review can then be a basis for some kind of action out of the available "arsenal". One such action is, of course, simple bans of particular applications or unconditional permissions. However, this is not the only actions available, and *should* not be if the price of precaution is to be possible to adjust according to the requirement of proportionality and contextual sensitivity. An alternative to simple banning is to decide on a moratorium and require the collection of better knowledge to mitigate knowledge gaps, and then reassessment in light of that knowledge. This action must, of course, allow some applications necessary to collect the new knowledge (otherwise the policy violates the requirement of non-paradoxicality). This kind of regulatory measure leads to the ethical issue of how much knowledge must be collected, and I have suggested that this issue should be assessed according to the same principles as those applied in the review. That is, a recommendation of delayed technology application and assembling of further information should itself be subjected to precautionary review to determine when the action is ripe for re-assessment. A third type of action is cautious permission, where some limit is set to the period the application may be used, after which a new assessment is made. The fourth action is conditional approval (unlimited in time) of use, requiring that the application is amended by safety measures of some sort. These may include barrier solutions to mitigate serious risks and uncertainties. As mentioned, this is an action that is mostly available in the early research stages of rather granular biotechnologies. Other solutions, which may be combined with barriers, are institutional arrangements of required review-milestones and other oversight measures (such as mandatory monitoring, inspections, submission of relevant measurements, et cetera). Of course, such additional requirements help to justify an application only if the additional costs and risks they effect do not undermine the reasons for allowing the application with the elevated safety level.

Finally, the pre-review system should also include a mechanism for having new and decided better biotechnologies not only be (conditionally) allowed, but to *actually replace* established and inferior

ones that have been identified through the review. This follows from the basic ethical requirements set out in section 3.2, and the immediate consequence that the age or novelty of an application is of no importance as such from a precautionary standpoint. As observed in section 3.4, having a perfect system in this respect may meet some pragmatic challenges, so this mechanism may have to be relaxed to allow a lingering presence of older biotechnological applications, as long as the risk and uncertainty profiles of these do not become unacceptable in view of the new technological possibilities. At some point, though, they should be expected to be phased out for precautionary reasons, and a good precautionary policy should provide mechanisms to stimulate such a development.

4.2 Variants 2 and 3: Simple bans and moratoria

These two variants differ from the pre-review variant in that they do not include nuanced assessment of individual applications, but deal with entire classes of technologies or applications. But structurally these regulatory variants are similar to variant 1, as they consist of an entry threshold, ethical standard and arsenal of action. The entry threshold specifies the type of technology or application in question, the ethical standard sets out why this type should be generally banned (unlimited or for some time), and the action is the type of ban applied. The presence of variants 2 and 3 in a precautionary regulatory system will elevate the price of precaution of this system, as will the actual discharging of the variant 2 and 3 mechanisms.

To be defensible from a precautionary standpoint, these variants must rest on an argument demonstrating that using the class of technologies or applications in question would be generally morally irresponsible. To be valid, such an argument must conform to the basic ethical requirements set out in section 3.2. Presumably, this implies that only very few classes of biotechnologies or applications in the non-human domain will be fitting for this type of regulatory action. These will presumably have either of two properties: (a) drastic knowledge gaps, (b) knowledge of very serious risks with no or only very limited compensatory benefits.

Typically, feature (a) will not justify a simple ban, but a moratorium, allowing for re-assessment at a later stage when more is

known. An exception would be if even basic research to promote better understanding of this class of technology or applications cannot be justified due to precautionary reasons (e. g. because the granularity and other properties of the technology makes safety arrangements very uncertain). When the time for re-assessment comes, the system enters a stage reminding of the review of variant 1, but looking at an entire class of technologies or applications. This may result in a continued moratorium, a phasing over to variant 1, or to a simple ban – all depending on the outcome of the assessment of knowledge gaps, risks and chances of benefit.

Feature (b), in contrast, may justify an unlimited ban on the basis that the class of technology or application is known to be irresponsible. If that is the case, it may be defensible to have the regulation target not only those applications that are the immediate source of the dangers, but also those uses that presuppose these applications (such as selling and consumption of products from a production assessed as irresponsible). However, as all knowledge may change, there may appear reasons with time that warrant a re-assessment, phasing the regulation over to more of a moratorium. As observed in section 3.3, such a change may also be warranted by changes in circumstances, as previously precautionary unacceptable technological solutions may become less irresponsible if alternative options seize to be accessible, feasible or are re-assed to be less responsible than before.

4.3 Combining the variants

In figure 3 is shown how all of the variants can be combined in a full policy. Any application in a concrete jurisdiction will, of course, need assessment of where to locate the entry threshold, make ethical standards concrete, and specify how to discharge different items of the arsenal of actions. As argued, these need to comply with the basic ethical requirements of section 3.2, and further need to decide on the weight of evil as described in section 3.3.

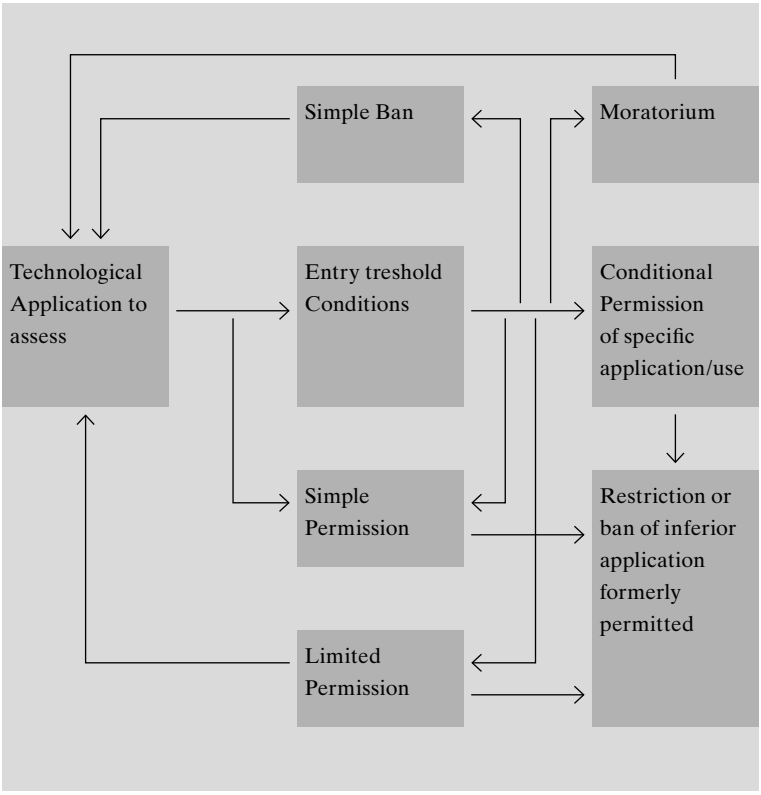
Simple Ban
Moratorium
Technological Application to assess
Entry treshold Conditions
Conditional Permission of specific application/use
Simple Permission
Restriction or ban of inferior application formerly permitted
Limited Permission

Figure 3

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