Environmental and Biosafety Research Ethics Committees: Guidelines and Principles for Ethics Reviewers in the South African Context

by

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DECLARATION

By submitting this thesis electronically, I declare that the entirety of the work contained therein is my own, original work, that I am the sole author thereof (save to the extent explicitly otherwise stated), that reproduction and publication thereof by Stellenbosch University will not infringe any third party rights and that I have not previously in its entirety or in part submitted it for obtaining any qualification.

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ABSTRACT

Over the last two decades, there was an upsurge of research and innovation in biotechnology and related fields, leading to exciting new discoveries in areas such as the engineering of biological processes, gene editing, stem cell research, CRISPR-Cas9 technology, Synthetic Biology, recombinant DNA, LMOs and GMOs, to mention only a few. At the same time, these advances generated concerns about biosafety, biosecurity and adverse impacts on biodiversity and the environment, leading to the establishment of Research Ethics Committees (RECs) at Higher Education and Research Institutions dedicated to reviewing research with implications for biosafety and the environment.

These Biosafety and Environment Research Ethics Committees, referred to as EBRECs, are in the early stages of their establishment and formalisation, and there is much uncertainty about their composition, scope, procedures of decision-making and the principles that should guide their deliberations and assessments. In many respects, EBRECs are venturing into uncharted territory, facing a very wide range of complex research fields, far-reaching research practices and deep concerns new to Review Boards, raising the question to what extent EBRECs can fall back on the fairly well-established principles and procedures of RECs focusing on Human, Health or Animal research, and to what extent they need new or adapted principles and procedures.

Against this background, I set out to answer the following three main research questions in this thesis:

1. What is the current state of ethical principles for ethics reviews in the field of environmental and biosafety research ethics? Which principles are currently used in this context, and how?
2. What are the shortcomings of the current principles used by EBRECs and how can they be overcome?
3. What ethical principles must be adopted by environmental and biosafety research ethics committees and guide them in their decision-making?

In order to prepare the ground and set the scene for my discussion of these questions, I also formulated four supporting research questions:

i. What is environmental research ethics in action?
ii. What is biosafety research ethics in action?

iii. How are environmental and biosafety ethics related to one another?
iv. How should the guidelines and ethical principles related to these two overlapping fields be implemented in the ethics review process?

Following my introduction and problem statement in Chapter 1, I devoted Chapters 2 and 3 to an overview of my supporting questions to set the scene for Environmental and Biosafety Research Ethics. In Chapter 4, I turned to my main research question with a discussion of national and international declarations, frameworks and legislation and an investigation of principles in the different research areas to get a picture of applicable principles that can guide EBRECs.

The main finding of my thesis is that due to the complexity of EBR, different categories of principles could be the solution for EBRECs. I elaborate on this in Chapter 5, my concluding chapter, in which I also propose a list of core principles that can serve as an accessible and easy-to-use guide for EBRECs in their decision-making. In this proposal, I cluster different kinds of principles in terms of four categories:

1. Principles as a Moral Concept
2. Principles as a Social Concept
3. Principles as a Legal Concept
4. Principles as a Safety Concept

OPSOMMING

Die afgelope twee dekades was daar 'n toename in navorsing en nuutheid op biotegnologie en verwante terreine, wat lei tot opwindende nuwe ontdekkings op gebiede soos die ontwerp van biologiese prosesse, geenbewerking, stamselnavorsing, CRISPR-Cas9-tegnologie, sintetiese biologie, rekombinante DNA, LMO's en GMO's, om maar net ’n paar te noem. Terselfdertyd het hierdie vordering kommer veroorsaak oor bioveiligheid, biosekuriteit en nadelige gevolge vir die biodiversiteit en die omgewing, wat gelei het tot die stigting van Navorsingsetiekkomitees (RECs) by hoëronderwys- en navorsingsinstellings wat toegewy is aan die hersiening van navorsing met implikasies vir bioveiligheid en die omgewing.

Hierdie etiekkomitees vir bioveiligheid en omgewing, waarna verwys word as EBRECs, is in die vroeë stadiums van hul stigting en formalisering en daar is baie onsekerheid oor die samestelling, omvang, prosedures van besluitneming en die beginsels wat hul beraadslagings en assesserings moet rig. In baie opsigte waag EBRECs op ’n onbekende gebied, met ’n baie wye reeks ingewikkelde navorsingsvelde, verreikende navorsingspraktyke en diep bekommernisse wat nuut is by beoordelingsrade en laat die vraag ontstaan in watter mate EBRECs kan terugval op die redelik gevestigde beginsels en prosedures van RECs wat fokus op navorsing oor mense, gesondheid of diere, en in watter mate hulle nuwe of aangepaste beginsels en prosedures benodig.
Met hierdie agtergrond in gedagte het ek die volgende drie hoofnavorsingsvrae in hierdie tesis probeer beantwoord:

1. Wat is die huidige stand van etiese beginsels vir etiese resensies op die gebied van omgewings- en bioveiligheidsnavorsingsetiek? Watter beginsels word tans in hierdie konteks gebruik, en hoe?
2. Wat is die tekortkominge van die huidige beginsels wat EBRECs gebruik en hoe kan dit oorkom word?
3. Watter etiese beginsels moet deur die etiekkomitees vir omgewings- en bioveiligheidsnavorsing aanvaar word en hulle lei in hul besluitneming?

Ter voorbereiding vir my bespreking van hierdie vrae, het ek ook vier ondersteunende navorsingsvrae geformuleer:

I. Wat is omgewingsnavorsingsetiek in werking?
II. Wat is navorsingsetiek vir bioveiligheid in werking?
III. Hoe hou omgewings- en bioveiligheidsetiek met mekaar verband?
IV. Hoe moet die riglyne en etiese beginsels wat verband hou met hierdie twee oorvleuelende velde in die etiek-hersieningsproses geïmplementeer word?

Na my inleiding en probleemstelling in hoofstuk 1, het ek hoofstukke 2 en 3 gewy aan 'n oorsig van my ondersteunende vrae om die toneel te stel vir omgewings- en bioveiligheidsnavorsingsetiek. In Hoofstuk 4 het ek my hoofnavorsingsvraag gewend met 'n bespreking van nasionale en internasionale verklarings, raamwerke en wetgewing en 'n ondersoek na beginsels in die verskillende navorsingsgebiede om 'n beeld te kry van toepaslike beginsels wat EBRECs kan lei.

Die belangrikste bevinding van my proefskrif is dat as gevolg van die kompleksiteit van EBR, verskillende kategorieë beginsels die oplossing vir EBRECs kan wees. Ek brei hieroor uit in hoofstuk 5, my slothoofstuk, waarin ek ook 'n lys van kernbeginsels voorstel wat kan dien as 'n toeganklike en maklik om te gebruik gids vir EBRECs in hul besluitneming. In hierdie voorstel groepeer ek verskillende soorte beginsels in terme van vier kategorieë:

1. Beginsels as 'n morele konsep
2. Beginsels as 'n sosiale konsep
3. Beginsels as 'n regskonsep
4. Beginsels as 'n veiligheidskonsep

DEDICATION

To my **parents:**
for always loving and supporting me.

To my **husband:**
for his unconditional love and care (keeping the household running and trying to understand the long hours).

To my **children:**
for believing in me.

To my **friends** and **colleagues:**
for supporting me and keeping my spirit high.

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LIST OF ABBREVIATIONS/ACRONYMS

Abbreviation/acronym	Meaning
ABSA	American Biological Safety Association
AI	Artificial Intelligence
ANR	French National Research Agency
ARC	Agricultural Research Council
AREC	Animal Research Ethics Committee
ARRIVE	Animal Research Reporting of In Vivo Experiments
ASSAf	Academy of Science of South Africa
BSL	Biological safety level
BSP	Biosafety Protocol
CBD	Convention on Biological Diversity
CERN	European Organisation for Nuclear Research
CIOMS	The Council for International Organizations of Medical Sciences
CoV	Coronaviruses
CRISPR	Clustered Regulatory Interspaced Short Palindromic Repeats
DALRRD	Department of Agriculture, Land Reform and Rural Development
DEFF	Department of Environmental, Forestry and Fisheries
DoH	Department of Health
EBR	Environmental and Biosafety Research
EBREC	Environment and Biosafety Research Ethics Committee
EuCheMS	European Association for Chemical and Molecular Sciences
EU	The European Union
FCD	Foodstuffs, Cosmetics and Disinfectants
GDPR	General Data Protection Regulation
GM	Genetically Manipulated
GMOs	Genetically modified organisms
GOFR	Gain-of-Function Research
IAEA	International Atomic Agency
IPBES	Intergovernmental Science-Policy Platform on Biodiversity and Ecosystem Services

IPEDR	International Conference on E-business, Management and Economics
IPPC	International Plant Protection Convention
iPSCs	Induced Pluripotent Stem Cells
***IRB(s)**	Institutional Review Board(s)
IUCN	International Union for Conservation of Nature
LIMICs	Low and Middle-Income Countries
LMOs	Living modified organisms
NCBI	National Center for Biotechnology Information
NEMA	National Environment Management Act (of South Africa)
NEMBA	National Environmental Management Biodiversity Act
NHREC	National Health Research Ethics Committee
NIH	The National Institute of Health
NIEHS	National Institute of Environmental Health Sciences
OECD	Organization for Economic Co-operation and Development
PBE	Principles of Biomedical Ethics
PETA	People for the Ethical Treatment of Animals
POW	Prisoners of war
PP	Precautionary Principle
PPPs	Potential Pandemic Pathogens
***REC(s)**	Research Ethics Committee(s)
RMS	Risk Mitigating Strategies
SANBI	The South African National Biodiversity Institute
SANS	The South African National Standard
SARS	Severe Acute Respiratory Syndrome
SATORI	Stakeholders Acting Together on the Ethical Impact Assessment of Research and Innovation
SCNT	Somatic Cell Nuclear Transfer
SOPs	Standard Operating Procedures
UFAW	Universities Federation for Animal Welfare
UK	United Kingdom
UN	United Nations
UNCED	United Nations Conference on Environment and Development
UNEP	United Nations Environment Program

UNESCO	The United Nations Educational, Scientific and Cultural Organization
UPOV	International Convention for the Protection of New Varieties of Plants
USA	United States of America
WEF	World Economic Forum
WHO	World Health Organization
WMA	World Medical Association
WWF	Worldwide Fund for Nature
WWII	Second World War
*REC and IRB are used synonymously in this study.	

DEFINITIONS

Artificial Intelligence: Artificial Intelligence and robotics are digital technologies that will significantly impact the development of humanity and the universe. It is the ability of a computer or computer-controlled robot to perform tasks commonly associated with intelligent beings, such as reason and decision-making, translation, speech recognition and visual perception (Copeland, 2020).

Biocontainment: The term refers to the various safety methods of managing infectious agents. The purpose is to eliminate and reduce environmental and human exposure to potentially harmful agents**.** Containment in research laboratories refers to the procedures and processes to confine harmful micro-organisms to the areas in which they are investigated. Primary barriers could be biological safety cabinets, enclosed containers or any other safety equipment. Secondary containment refers to protecting the environment outside laboratories from exposure to infectious materials (Medical Dictionary, 2009).

Bioethics: This term refers to study of the ethical and moral implications of biological discoveries, biomedical advances and their applications (WHO, 2006). Bioethics within the life of sciences is not limited to animal and clinical research ethics but encompasses many interlinking areas of responsible conduct of research, including obligations to society, responsibilities towards creation of beneficial research and avoidance of maleficence (ASSAf, 2015).

Biohazard: Or biological hazard is a biological material or substance that constitutes a threat or hazard to the health and safety of humans, animals, plants or the environment (Shroder & Sivanpillai, 2015: xxi).

Biological material: refers to micro-organisms, proteins and nucleic acids along with other biological matter that may contain bacteria, viruses, unicellular organisms, proteins and nucleic acids, whether or not they are infectious or toxic. This material may pose a risk to health and safety or the environment (CBH, 2016: 6).

Biorisk: "(Risk is a function of likelihood and consequences). The risk of occurrence of a particular biological event (including naturally-occurring diseases, accidents, unexpected discovery, or deliberate misuse of biological agents and toxins) which may adversely affect the health of human populations" (ASSAf, 2015). But the term is also frequently used for various purposes not only regarding human health but also including risk to the environment or risk associated with biological material and infectious agents in the laboratory due to an adverse event that may lead to harm (WHO, 2006: iii).

Biosafety: Prevention of large-scale loss of biological integrity – refers to all aspects of containment to prevent exposure to or accidental release of biohazards. Also, the safe development, application and utilisation of biotechnology and its products (UNEP-GEF BCH Project, 2011: 13).

Biosecurity: "… refers to measures to protect against the inadvertent, inappropriate, intentional and malevolent use of (potentially) dangerous biological material (including pathogens and their products) or the malevolent use of biotechnology against livestock or crops. This also includes the protection of valuable biological material" (WHO, 2006; ASSAf, 2015).

Biotechnology: refers to any technological application that uses biological systems, living organisms or derivatives thereof to make or modify products or processes for a specific use.

Traditional Biotechnology includes commonly known fermentation techniques to make beer, cheese or bread. Alternatively, conventional breeding techniques can include those for animals and plants such as hybridisation and specific characteristics selection to create better crops. With **Modern Biotechnology,** researchers can now take a single gene from an animal or plant cell inserting it into another plant or animal to confer desired characteristics such as resistance to a specific pest or disease (UNEP-GEF BCH Project, 2011).

Dual-use life sciences research: Knowledge and technologies generated by legitimate life sciences research that may be appropriated for illegitimate intentions and applications (WHO, 2005; ASSAf, 2015).

Environmental Research Ethics: is all about balancing scientific and ethical commitments and the environmental scientists' obligation to protect not only human interests but also the non-human world (Harman et al., 1998: 278). Furthermore, it “is the discipline in philosophy that studies the moral relationship of human beings to, and also the value and moral status of, the environment and its non-human contents. [Environmental ethics] covers [among other themes] … the attempt to apply traditional ethical theories, including consequentialism, deontology, and virtue ethics, to support contemporary environmental concerns; … the preservation of biodiversity as an ethical goal; … broader concerns … with wilderness, the built environment and the politics of poverty; … the ethics of sustainability and climate change, and … some directions for possible future developments of the discipline" (Stanford Encyclopedia of Philosophy, 2015).

Ethics Dumping: This is the practice in which researchers from wealthier countries with strict regulations move the risky research to lower-income settings with laxer laws and thus face less difficulty getting permission to carry out that research. The exportation of these non-

compliant research practices is called ethics dumping. The EU coined the phrase “ethics dumping” (European Commission, n.d.). Ethics dumping occurs mainly in two areas. “First, when research participants and/or resources in low- and middle-income countries (LMICs) are exploited intentionally, for instance, because research can be undertaken in an LMIC, that would be prohibited in a high-income country. Second, exploitation can occur due to insufficient ethics awareness on the part of the researcher or low research governance capacity in the host nation” (Schroeder, 2018: 2).

Gain-of-function (GOF) research: This is research that "involves experimentation that aims or is expected to (and/or, perhaps, actually does) increase the transmissibility and/or virulence of pathogens". Thus, research that can pose biosecurity and biosafety risks (Selgelid, 2016: 1).

Laboratory Biosafety: "… refers to practices, procedures and proper use of equipment and facilities, in order to assure the safe handling, storage and disposal of (potentially) harmful biological material (including pathogens and their products)” (WHO, 2006). This includes measures to prevent harm caused by inadvertent or accidental exposure to dangerous pathogens and toxins (ASSAf, 2015).

Lacunae: Means an unfilled space or gap. In research, it describes an area of science that has not been studied but has the potential to be studied scientifically because it falls between different areas of science and not within a single discipline of science (Oxford Dictionary).

Life sciences: "All sciences that deal with organisms, including humans, animals and plants, and including but not limited to biology, biotechnology, genomics, proteomics, bioinformatics, pharmaceutical and biomedical research and techniques" (ASSAf, 2015).

Living Modified Organism (LMO): "Any living organism that possesses a novel combination of genetic material obtained through the use of modern biotechnology" (The Cartagena Protocol on Biosafety, 2000).

Pathogen: A micro-organism that causes or can cause disease. A microbe that can "cause damage in a host". A disease-producing agent such as a virus, bacterium or other micro-organisms (NCBI website).

Stem Cells: These are special cells with the unique ability or capacity to self-renew and generate multiple specialised cells within the body. Human stem cells can come from an adult human or an embryo. Stem cells have the potential to replace defective or damaged cells and can be used for the development of therapies (NIH website).

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CHAPTER 1: ORIENTATION, BACKGROUND AND PROBLEM STATEMENT

1.1 Background and introduction

I wrote the bulk of this thesis under conditions of lockdown in 2020 while the Covid-19 pandemic ravaged South Africa. With the rationale for this lockdown being an endeavour to curb the spread of the new Coronavirus, one would be hard-pressed to find a more dramatic reminder of the utmost importance in our time of biosafety and environmental care. While the pandemic tightened its grip on the world, we struggled to comprehend the enormity of the situation. We all continue to seek answers, and many theories and narratives arise. The two prominent theories, both unconfirmed as yet, about the origin of the virus are (a) an unfortunate escape from a research library and, and (b) risky human-animal interaction within the context of a disturbed environment.[1] Only time and research will eventually unravel the mystery of the true origin. In the meantime, scientists and researchers work frantically to find out more about the virus, how to contain it and what the best vaccination regime against the virus is. In its own right, this search for vaccinations and the continuing research around its safety and efficacy brought about its own challenges for ethical research and review processes in research ethics committees.

All of this puts biosafety and environmental care squarely on the agenda of state authorities and researchers directly concerned with the immediate task of responding to Covid-19, but also in more general terms on all research in which the environment and biosafety are likely to be implicated. In this thesis, my focus will be on the ethics clearance processes of research in which the environment and biosafety are at stake. While the ethical review of biomedical and human research has become a well-established practice over decades, the same is not true of research ethics processes regarding the environment and biosafety. Environment and Biosafety Research Ethics Committees (EBRECs) are a fairly recent development, and its frameworks, principles and procedures are, first, not well-established and, second, barely researched. This thesis aims to take a few steps towards filling this gap.

[1] Coronavirus disease 2019 (Covid-19). At the start of the Coronavirus outbreak near the end of 2019, the mainstream assumption was that the virus originated from a so-called wet market in Wuhan – the Chinese city where the first Covid-19 cases were reported, and bats were mentioned as the original source. The virus is zoonotic, meaning transmitted from animals to people. But as the virus started to spread globally, the role of public-health laboratories in Wuhan came under scrutiny. These labs could identify that coronavirus most likely come from the nocturnal mammal, but the same labs fuelled biosafety concerns and there were even worldwide claims that it was engineered by scientists. Many other viral conspiracy theories have been spreading globally since it was acknowledged as a pandemic (Abaido & Takshe, 2020: 122–124).

Research ethics is a specialised discipline and requires clear ethical guidelines and principles to guide researchers, research ethics committees and research ethicists. These guidelines and principles, however, were not clear from the start. They emerged over time and went through a number of iterations as they were clarified and institutionalised in different research fields. Research ethics was initially only associated with the medical field and to protect human participants, it only emerged in the other sciences much later.

The Second World War (WWII) can be considered as an important landmark in the history of research ethics due to the experiments in the Nazi concentration camps and on prisoners of war (POW). Although the research during that period arguably provided valuable results in certain instances,[2] in many cases including experiments that yielded valuable data, it caused injury and death to the participants.[3] These unethical research practices led to the Nuremberg Code in 1947. This was the first international document defending voluntary participation and informed consent of research participants. In the aftermath of the Nuremberg trials, the World Medical Association began drafting recommendations for human biomedical research in the form of the Geneva Convention (1949) and the Helsinki Declaration (1964). However, these codes and guidelines were not enough to prevent the abuse of research participants in the post-war years.[4]

The establishment of formal research ethics committees (RECs) and the review of research proposals started after a recommendation by the World Medical Association in 1975 to protect human subjects from unethical, inhumane and cruel research practices in biomedical research (Mandal, 2011: 2; Hansen, 2015: 3–4). Research ethics thus originated in North America and Europe (Nicholls, 2015: 1), but in South Africa, the University of the Witwatersrand already established the first REC in 1966. (Cleaton-Jones, 2019: 200). Today commencement with

[2] Nazi doctors had unfettered access to human beings for medical experiments that was mostly just another form of mass torture and murder, but it posed a moral challenge regarding some medical experiments that produced scientifically sound data. An example is the hypothermia experiments where people were immersed in ice water until they became unconscious or died. This provided useful data about the success rate of re-warming. This data were cited in scientific papers from the 1950s–1980s but without any indication of source or nature. Currently, however, the use of such data are mostly rejected by publishers if the source is known to be the Nazi experiments. Thus, the question can be asked if good can be derived from a wrong doing? (Gillam, 2015).

[3] Many examples of bad and/or unscientific, unethical experiments can be mentioned but the experimentation of Josef Mengele furnished him with the name “Angel of Death” due to his inhumane experiments on human twins at Auschwitz. Between 1943–1944 Mengele performed terrible experiments without anaesthesia on 1500 sets of twins. Experimentations included blood transfusion between twins, isolation, injections with germs, sex change operations, removal of limbs and organs and incestuous impregnations (*cf.* Bekier, 2010).

[4] The Guatemala Syphilis and Gonorrhoea experiments between 1946–1948 involved 696 male prisoners and female patients and was conducted without their knowledge or permission. What is even more shocking is the fact that these unethical experiments were co-sponsored by the NIH in the USA, the Pan American Health Organization and the Guatemalan Government. “These experiments were considered, approved and initiated only a year after the trial of the Nazi doctors” (Pecorino, 2002). The Tuskegee Study of Untreated Syphilis in the Negro Male that was conducted between 1932, and 1972 is a similar case in point.

research on humans and animals cannot proceed without ethical clearance; it is a global and legal requirement.

On the other hand, research ethics in natural sciences only gained some recognition in 1997 when Joseph Rotblat, a Nobel Prize winner and Polish physicist, suggested an ethical code for scientists. The code was to raise awareness for scientists' social and moral responsibilities in other non-medical, scientific and non-human fields. The philosopher Karl Popper also promoted an ethics oath for scientists while Rotblat tried to establish an international ethics committee in 1997 to monitor natural science research. Rotblat failed because researchers saw this as a risk for scientific advances (Hansen, 2015: 4).

In South Africa, the same arguments mentioned above were raised. Diana-Abasi Ibanga, researcher and philosopher from Nigeria, argued in an article in 2018 that research ethics, specifically environmental ethics, is still a developing area in Africa. He also indicated that few scholars have contributed to establishing a "theoretical basis of the discipline in terms of determining its comprehensive philosophical aspects" and its practical applications (Ibanga, 2018: 124).

The ethics of research and the integrity of research require adherence to the ethical principles and standards for the responsible conduct of research. Ethics reviews and ethics clearance are thus the first and most important actions of the research process to help ensure exactly that.

According to the Singapore Statement on Research Integrity,

> [T]he value and benefits of research are vitally dependant on the integrity of research. While there can be and are national and disciplinary differences in the way research is organised and conducted, there are also principles and professional responsibilities that are fundamental to the integrity of research wherever it is undertaken (The Singapore Statement[5], 2010).

The research ethics committee has the momentous task of conducting a critical and detailed review of a research proposal because of the severe and unfortunate implications of unethical research. According to Human-Vogel and Coetzee (2011: 167), ethics reviews in research are "a necessary social practice that serves to encourage researchers and institutions to be accountable".

Dr David Resnik, a Bioethicist and Institutional Review Board Chair at the NIH, gives some reasons why it is crucial to adhere to ethical norms in research. According to him, it promotes the aims of the study, it helps to ensure accountability to the public or community and helps

[5] Guidelines such as these are not included in the reference list but in Appendix B.

build public support. If the integrity and quality of research can be trusted, funders will also be more willing to fund the research (Resnik, 2015: 1).

Thus, the research process can only start when an ethics committee has confirmed that the research is ethically sound and can go ahead according to an approved research plan or protocol. In this regard, codes, policies and guidelines are vital and valuable for decision-making by research ethics committees, but similar to any set of rules, they do not cover every situation and sometimes conflict. In most cases, ethical decision-making in research ethics committees require considerable interpretation. In this regard, while researchers, reviewers and ethics committees rely on ethical principles, they also need to learn how to interpret, evaluate and apply the principles.

Human research ethics is primarily about people and our responsibility towards them. Globally clear and strict principles are applicable to review the research process when humans are involved. Research ethics committees worldwide accept multinational and multidisciplinary guidelines and principles to guide them in the ethical decision process. The first international instrument was the Nuremberg Code (1947) and shortly after this code, the United Nations (UN) adopted the Universal Declaration of Human Rights (1948). In 1964, The Declaration of Helsinki, issued by the World Medical Association, was introduced as a fundamental document in biomedical research. It also influenced international legislation and codes of conduct. The Singapore Statement (2010) was also endorsed globally. The Council for International Organizations of Medical Sciences (CIOMS) and the World Health Organization (WHO) provided further global ethical guidance on clinical trials (CIOMS, 2002).[6]

In South Africa, The National Health Research Ethics Council (NHREC) was established in 2006 in terms of the National Health Act (NHA) as the regulatory authority for all Human and Animal Research Ethics Committees (NHREC, 2015: 9). In the guidelines that they provide for ethical research on humans and animals, they explicitly refer to norms and standards for A) health research involving humans and animals as well as for conducting clinical trials. B) determine guidelines to facilitate best practice for research ethics committees (NHREC, 2015: 9) and C) register and audit RECs that review research involving human participants and ARECs that review research using animals (NHREC, 2015: 11) The NHREC emphasises the following broad ethical principles for human research a) beneficence and non-maleficence, b) distributive justice (equality) and c) respect for persons (dignity and autonomy) (NHREC, 2015: 14–15).

[6] Links to these international and other guidelines are provided in Appendix B.

Ethics regarding animal welfare and animal use in research are also well covered with the globally accepted 3Rs principles: Replace, Reduce and Refine. Charles Hume, the founder of the Universities Federation for Animal Welfare (UFAW), first proposed the 3Rs principles when conducting a scientific study in laboratory animal experiments in 1954. W. Russell and R.L. Burch also proposed the 3Rs principle in 1959 for the ethical use of animals in research in their book, *The Principles of Humane Experimental Technique*. These famous principles are now firmly embedded as standard practice in the conduct of animal-based science throughout many countries in the world. Ethics committees in Animal Research accept and apply these three principles globally (Tannenbaum & Bennett, 2015).

In 2010 the *Animal Research Reporting of In Vivo Experiments Guidelines* (ARRIVE) were published in the UK as an additional framework to improve the quality of animal research. Later in 2017 in a publication of Aske and Waugh (2017: 1491, 1492) they presented two more Rs, namely, Rigour and Reproducibility, expanding the 3R into the 5R principles to improve the transparency and quality of animal experiments. This implicated that animal studies must also adhere to scientific rigour, experimental design and methods that are robust and unbiased, and that experiments, results and reporting methods must be transparent. This ensures more reproducibility and transparency in animal research (Aske & Waugh, 2017: 1491).

Within the South African context, the South African Bureau of Standards of 2008 prescribes the minimum uniform national standards applicable for research on animals in South Africa, all based on international standards for the protection of vertebrate animals used for scientific study and other scientific purposes. [7]

On the other hand, environmental ethics only emerged in the early 1970s as an academic field, when it was acknowledged that nature, ecosystems and the biosphere are also vulnerable to human impacts in general (Palmer *et al.,* 2014: 421) and certain scientific research in particular. Different environmental theories were explored over the years, and

[7] For the purposes of this thesis I do not engage with the extreme position that all animal research should be abolished, as PETA (People for the Ethical Treatment of Animals) promote. My position is rather that scientific research on animals cannot be avoided and that the use of animals in research needs careful consideration. While it can be generally accepted that it may be necessary to use laboratory animals to create improvements for people, animals and the environment, (Rollin, 2007) I agree that it is also generally accepted that animals have a moral status and that the way they are treated in research should be subject to ethical considerations. For the purposes of my thesis I therefore assume that ethics reviews for research on animals are required and that the ethics review should at least reflect the following: (i) that animals have a moral status that must be respected and that the welfare of animals in research projects should always be considered; (ii) that animals are sentient creatures with the capacity to feel pain or distress and that the interests of animals must therefore be taken into consideration. The care and use of animals for scientific purposes in research, testing, teaching and education are described in the *South African National Standard Document* (SANS 10386: 2008).

environmental ethics has become a prominent discussion area worldwide (Palmer *et al.,* 2014: 421–422). However, the literature on guiding principles in environmental and biosafety research ethics is not well developed or refined. Ethics principles in environmental and biosafety research (EBR) are indicated in a few articles[8] only that will be discussed in the chapters to follow, but a set of globally accepted principles, as is the case with human- and animal research, is hard to find. As I will discuss in later chapters, environmental- and/or biosafety ethics literature, indicating ethical principles for research in these fields are very fragmented and mostly field specific.

Biosafety ethics mainly deals with integrity in biological and biotechnology research and often is, or should be, combined with environmental ethics. The research ethics committees in these fields typically review and approve research potentially hazardous to humans, animals or the environment. The National Institute of Environmental Health Science (NIH) in the USA is the leader in this field and an international registration body where EBRECs may register. The NIEHS is one of the NIH's 27 institutes and centres and acts as a foundation of supportive resources, assisting with training and strategies for research innovation and discovery (NIEHS, n.d.). However, it is important to note that Environmental and Biosafety Ethics committees in South Africa register with the NIH due to the lack of a national registration body in South Africa to oversee environmental and biosafety research ethics. The Academy of Science of South Africa (ASSAf), started in 1996, encompasses all fields of scientific work for the South African context, but they are not a registering body for ethics committees. ASSAf aims to "provide evidence-based scientific advice on issues of public interest to government and other stakeholders" (ASSAf, n.d.). Furthermore, only a few higher education institutions in South Africa have a registered Environment and Biosafety Ethics Committee, while some institutions only have a Biosafety Committee that oversees biosafety risk factors and laboratories. [9]

A complicating factor in this field is that EBR covers a vast range of disciplines, in physical and life sciences, engineering, computer sciences and many more that will be discussed in this study. Modern Biotechnology is a new field that promises advances in medicine, agriculture and many other fields such as vaccines, medical treatment, improved crops and new industrial products. In this new field, much about the interaction of GMOs and LMOs and

[8] See for example Gandhi (2015), ASSAf (2015), Beckett (2017), Müller (2020), Resnik (1998) and Uppsala (1984).

[9] The University of the Witwatersrand, the University of Cape Town and the University of KwaZulu-Natal have a Biosafety Committee that are registered with the NIH. Stellenbosch University and the University of the Free State have an Environmental- and Biosafety Committee that are also registered with the NIH. No other registered South African institutional committees for Environmental- and/or Biosafety ethics could be identified when this study was conducted (NIH verified).

their influence on ecosystems are not yet known. The vast range of disciplines in biotechnology and biosafety even include research on artificial life forms or artificial intelligence (AI) and robots. AI can be programmed to perform many beneficial actions but achieving it using a destructive method. For example, a geo-engineering project where a super-intelligent system is tasked might cause havoc with the ecosystem. The AI will be programmed to accomplish its goal, but if the purpose, for example, is not aligned with the ecosystem, it can cause serious problems.

Therefore, any research institution dealing with biotechnology, biological material as well as other areas in the environmental and biosafety fields need to have an ethics committee, and furthermore, clear guidelines and well-articulated ethical principles should guide those institutions that already have such an ethics committee to deal with research proposals in this complicated and broad field in the natural sciences. It is, however, important to note that there are no clear boundaries or indication of what research will fall under the EBRECs responsibilities and what scope they have. Internal procedures that EBRECs at higher education institutions should follow in their reviews of research protocols are also unclear and institutions with EBRECs are still trying to figure this out. To deal with this question will fall outside the scope of this study and will probably be suitable for a full length PhD in its own right. Therefore, I acknowledge the challenges in this regard and hope this can be dealt with in another study.

However, there is a dire need to explore and investigate the ethical principles relevant to Environmental and Biosafety Research Ethics, and there is an equally dire need to contextualise such principles within South Africa, as it is confirmed by the recent study and report of ASSAf (2015) on the *State of Biosafety and Biosecurity in South Africa*. This report indicates that well-formulated guidelines in this field have been lagging behind relative to the well-formulated guidelines for human- and animal research in South Africa (ASSAf, 2015: 27). The report also stated that much work must still be done to improve the current situation in South Africa: “In South Africa, no guidelines specifically formulated for life sciences that do not entail research on human participants have been formulated or published” (ASSAf, 2015: 81). [10]

With this background in mind, I can now turn towards my problem statement.

[10] “South Africa should establish clear, encompassing and balanced ethical guidelines for all life science research and development work to ensure our safety and integrity of the environment we live in” (2015: 28).

1.2 Problem statement

As indicated in the background sketch above, the primary responsibility of a research ethics committee should be the assessment of all the ethical aspects of a research proposal to guide the researcher in the research process. Ethics committees deal with the review and approval of research proposals in order to determine whether appropriate ethical principles and values are applied and ultimately to help ensure that the goal of socially and environmentally responsible research is achieved. Clearly defined principles supported by transparent and explicitly formulated notions of the theoretical assumptions, values and the moral course of action associated with these principles promote the quality and integrity of the research and assist the ethics committee in formulating justifiable, consistent and fair proposal reviews.

It is a matter of great concern, though, to note the virtual absence of clearly defined ethical principles and norms in the complex and multidisciplinary fields of research that can have detrimental impacts on the environment and biosafety. As the Cartagena Protocol confirms: "… the stakes are high, […] humanity is pushing ecosystems, species and gene pools to extinction …" and "while modern biotechnology may have great potential, it must be developed and used with adequate safety measures, particularly for the environment" (The Secretariat of the Convention on Biological Diversity, 2000).

This situation raises many entangled ethical, environmental, social as well as health issues, which include questions about the conservation and sustainable use of biodiversity and a recognition of the potential of modern biotechnology to improve human well-being. However, contemporary biotechnology could have serious effects on the environment, societies, human well-being and health. The Covid-19 global pandemic is a revelation in this regard and a confirmation that we need legally binding national and international biosafety instruments as guidance. This also gives rise to the challenge of integrated thinking and possibly even new approaches to research activities and, in particular, to the implementation of the research ethics review process. A case-by-case approach in a good review process, combined with scientific assessment and substantive risk mitigation, guided by clear ethical principles, is clearly of the utmost importance.

Based on the above, the task that I have set for this study is:

1. to determine the current state of ethical principles in environmental and biosafety research ethics;
2. to determine the shortcomings of current and existing ethical principles used in research with environmental and biosafety implications; and
3. to determine the ethical principles that should guide environmental and biosafety research ethics.

Problem areas that contribute to the issue that will be tackled in this study are the lack of a national regulatory authority and the lack of well-established and trained environmental and biosafety ethics committees in South Africa. With my investigation, I hope to take the first steps towards filling this gap and to underline the importance and complexity of environmental and biosafety research ethics and its multidisciplinary aspects; something that I firmly believe should be acknowledged by our national authorities, higher education institutions and Science Councils.

1.3 The aim of the study

This study aims to find and develop a framework of applicable ethical guidelines and principles to enhance and refine the ethical review and decision-making process for EBRECs. This is envisaged to guide researchers, ethics committee members, ethics reviewers and ethicists involved in this process.

In this regard and more narrowly defined, I aim to formalise a set of principles for EBRECs that can assist within a South African context. I envisage that the results of this study will be of value to different role-players in research ethics:

- to the researcher – to be protected and informed of possible moral and ethical issues;
- to the ethics committee – to ensure depth, rigour, consistency and accountability in reviews and approvals;
- to the reviewer of a research proposal – to provide relevant recommendations based on a uniform framework;
- to the ethicist – to guide in complex ethical dilemmas that may arise in specific research fields;
- to research administrators – to ensure a fair and open ethical process; and
- to external parties such as sponsors who may have an interest in the research – to ensure transparency and trust in sound ethical practices in the research process.

I also envisage that the results of this study will be of interest to research environments and societies that the EBRECs decisions could influence.

To achieve the aims of this study, existing literature on the topic will be reviewed and available guidelines and approaches explored. Furthermore, the different strategies regarding guidelines and principles will be discussed to determine the most applicable frameworks and principles. The final aim will then be to formalise a proposed set of principles for the South African context or scenario.

1.4 Research questions

The online Encyclopaedia of Philosophy distinguishes between three major areas of ethics studies: 1) Applied ethics, which defines what should be done in a specific domain, situation or area; 2) Normative ethics, which determines the general standards we set for morally acceptable courses of action and; 3) Meta-ethics, also called theoretical ethics, which determines where our ethical principles come from and what their "truth value" is: "Are they merely social inventions? Do they involve more than expressions of our individual emotions?" In short, in meta-ethics, questions about the cognitive status of ethical principles and judgements are asked, among which is the question of whether ethical principles capture universal truths or not (Fieser, 2020: 1).

Research ethics incorporates all three of these areas. Still, for the purposes of this study, I will focus mainly on questions from the second, intermediate level, namely normative ethics. However, I will not entirely exclude questions and considerations from the other two levels of ethics in my discussion. To be specific, in the ethics review process, the aim is to make clear distinctions between research that is ethically acceptable or unacceptable, or to identify ethical risks[11] that researchers should avoid – also proposing ways and means to prevent or mitigate such risks. These specific recommendations in the context of a particular case or research proposal fall within the ambit of applied ethics. At a deeper level, though, these practical recommendations on what should be done (or not done) are all motivated and informed by *reasons*. These reasons are usually articulated in terms of applicable ethical principles. Deliberation about the meaning and application of such ethical principles, in turn, fall within the ambit of normative ethics and this forms a big part of the discussions typically encountered in ethics review committees.

Further and more profound questions about the justification of ethical principles and what counts as a sound justification fall within the field of meta-ethics, but this is not what this study is all about. The latter kind of discussion takes one into very deep philosophical waters, while the research questions of this study are articulated on a more practical and normative level. They are the following:

- What is the current state of ethical principles for ethics reviews in the field of environmental and biosafety research ethics? Which principles are currently used in this context and how?

[11] Ethical risk refers to unexpected negative consequences of unethical actions. A researcher could be unaware of unethical aspects of their action especially when actions are in self-interest and the possible negative consequences cannot be anticipated. For the purpose of Research Ethics, it includes the following actions: identification, mitigation and transformation of the ethical risks (Le Menestrel, 2011; 2015).

- What are the shortcomings of the current principles used by EBRECs and how can they be overcome?
- Which ethical principles must be adopted by environmental and biosafety research ethics committees and guide them in their decision-making?

In order to answer these questions, there are numerous further supporting questions, more of a factual nature, that I also need to get clarity on, and they are the following:

- What is environmental research ethics in action?
- What is biosafety research ethics in action?
- How are environmental and biosafety ethics related to one another?
- How should the guidelines and ethical principles related to these two overlapping fields be implemented in the ethics review process?

In the next section, I give an overview of the methodology I will follow in my effort to answer these questions.

1.5 Methodology

The methodology followed in this non-empirical, desktop study was an exploratory approach, incorporating an intensive and critical survey and interpretation of relevant literature and writings on the subject. Literature sources consisted of, but were not limited to, articles, reviews, academic papers, journals, books, web articles, conference proceedings and reports. Furthermore, numerous international codes, declarations, reports, statements, conventions, protocols, frameworks and guidelines were scrutinised; a comprehensive list of which is provided in Appendix B.

I will use the term “Environmental and Biosafety research ethics” in the broad and encompassing sense to include all related terms in the natural, biological and chemical sciences, e.g. ecological research ethics, geo-ethics, eco-ethics, agricultural ethics, earth sciences, etc. The literature review included an investigation into the standard operational procedures of higher education institutions globally that have a registered Environmental and Biosafety Board/Committee.

In my search for relevant sources, I conducted keyword searches in the primary and most accessible electronic research databases; the results of which are discussed in the chapters that follow. The following electronic databases were screened: EBSCOhost; NRF Current and Completed Research; Science Direct; Web of Science; Glob-ethics.net, and the Academic Search Ultimate (Multidisciplinary database). All the searches included results from 1970–2020.

The six databases selected are well-known and widely recommended in the research community. Nine initial and general searches were conducted with keywords to include *"research ethics", "environmental and biosafety research ethics"*, *"human- and animal research ethics"*. Nine advanced searches were eventually conducted, using the same initial keywords as indicated, but in combination, e.g. *"Environmental AND Biosafety Research Ethics"* AND *"Ethics Committee".* The aim was to identify the number of published articles under the various selected keywords through a quantitative methodology approach. These quantitative searches confirmed how small the number of studies are that focus on the ethical principles and the ethical review processes of EBRECs. [12]

1.6 Outline of study

Having explained the aims, objectives and methodology of this research against the background and the problem statement of my research, the outline of my chapters in this study will be as follows.

Chapters two and three will set the scene for environmental and biosafety research ethics, explaining the meaning of research ethics and providing an outline of the history and development in the relevant ethics fields. These chapters briefly indicate how they generate pertinent questions but also values and principles relevant to the research ethics process in general. The chapters also touch on general theories and frameworks in the ethical decision-making process. International frameworks and protocols that are universally applicable, accepted globally and adapted for local and cultural values, also come under the microscope to determine how they relate to environmental and biosafety research. Then my focus will shift to the more specific topic of approaches and principles for ethical assessment and an overview of ethical issues in environmental and biosafety research ethics, which will be the main topic of discussion in these chapters. In this context, national and international regulations, legislation and declarations relevant to research ethics concerning environmental and biosafety research will be investigated. The last section of chapter three deals with special considerations that need to be considered in research ethics, such as risk assessment and risk management, which is a crucial focus in environmental and biosafety research ethics.

In chapter four, I will refine my analysis by focusing on the principles for research ethics processes in various countries and disciplines around the world. In this discussion, I will identify the strengths regarding these principles and any problems and gaps they may have. Accordingly, this will serve as a platform to propose the framework, approach and principles relevant to ethics clearance processes of environmental and biosafety research. Specific

[12] Refer to Appendix A for the Quantitative Research Results.

principles that should guide Environmental Research Ethics and Biosafety Research Ethics and the justification for the proposed principles will be discussed.

Chapter five, the last chapter of the study, will conclude with a recommendation regarding the ethical principles and a suitable framework applicable to the South African context in EBRECs. Themes for further investigation will also be delineated.

CHAPTER 2: SETTING THE SCENE FOR ENVIRONMENTAL AND BIOSAFETY RESEARCH ETHICS – I

2.1 Introduction

Chapter 1 distinguished between the main research questions of this study and some supporting research questions that provided the foundation and background and will help me answer the main research questions. With the ultimate aim of this study being to address the gaps and challenges in reviewing research in the fields of biosafety and the environment, this chapter will be devoted to defining and explaining what environmental and biosafety research (EBR) ethics entail. This chapter covers three of my supporting questions: *1) What is biosafety research ethics in action? 2) What is environmental research ethics in action? and 3) How is EBR ethics related to one another in various research activities and disciplines?*

As such, this chapter will set the scene and reinforce the context to understanding the history, dynamics and interrelations of this complex, transdisciplinary and interdisciplinary field. I will give an overview of related terms and meanings and will discuss research activities with practical examples from the respective fields of environmental and biosafety. I also will highlight sensitive areas and ethical concerns related to this research, and I will reflect on the role and challenges of EBRECs and then conclude with a summary.

2.2 Introduction to environmental and biosafety research ethics (EBR)

In environmental research ethics, the focus is predominantly on safeguarding species, habitats and ecosystems, and ensuring a healthy environment with biological richness, taking into account the biodiversity of the Earth, as well as the variety of human interests supported by healthy and ethical human-environment interactions. As such, environmental research ethics is all about balancing scientific and ethical commitments and the environmental scientists' obligation to protect not only human interests but also the non-human world (Harman *et al.,* 1998: 278). This means that environmental research ethics, to a large extent, forms part of environmental ethics in general; the aim of which is to provide moral motivation and ethical justification for environmental protection globally.

It is a well-known fact that humans strive to tame all forms of life on Earth and not always in the best interest of the environment. Since humans' existence, natural diversity is manipulated and exploited to derive benefits from nature for survival and well-being (Christoffersen & Mathur, 2005: 255). In recent years the rapid advancement in sciences, technology and biotechnology has brought many new and confounded ethical challenges, as I have alluded to in Chapter 1. Researchers are constantly working towards better solutions to improve or

change life on Earth to enhance human lives and solve problems. The character of research ethics thus changed from typically a simplistic researcher and research subject relationship in the 20th century to a relationship with multiple levels in the 21st century. The fourth industrial revolution brings new unanswered questions and ethical challenges are multiplied. Part of the problem, however, is the difficulty that scientists themselves experience in recognising these challenges and realising that research itself is a value-laden enterprise that should be recognised and acknowledged as such. Resnik (as cited in Brall *et al.,* 2017: 33) explains these difficulties when he argues "… that even though science is deemed objective, evidence-based, and 'value-free', it nevertheless involves researchers' epistemic and non-epistemic values".

Higher education institutions (HEIs) in South Africa take the lead in technological advances, research and innovations. The two broad research areas that fall under the scope of EBRECs in HEIs can be divided into *1) Physical Sciences and Engineering* and *2) The Life Sciences.* Physical Sciences and Engineering include the following type of disciplines: Chemistry, Chemical Engineering, Computer Science, Earth and Planetary Sciences, Energy Studies, Engineering, Materials Sciences, Physics and Astronomy. Life Sciences is an enormous field that examines every living thing on Earth; it includes Agricultural and Biological Sciences, Biochemistry, Genetics and Molecular Biology, Environmental Science, Immunology and Microbiology.[13]

Research at HEIs varies from foundational science to new and novel research, covering an extensive range of disciplines and moving from the theoretical to the applied. For distinctness and the study's purpose, all the areas mentioned above will be covered under the term EBR (Environmental and Biosafety Research). I have indicated in Chapter 1 that Environment and Biosafety Committees (EBRECs) at HEIs in South Africa are a fairly new development, and not all the HEIs have a registered committee. However, some institutions do have an Institutional Biosafety Committee (IBC). For the purposes of this study, I will use the term EBREC to include both scenarios.

2.3 EBR ethics in action in higher education institutions: Life sciences, physical sciences and engineering

According to the Massachusetts Institute of Technology, the convergence of Life Sciences, Physical Sciences and Engineering is the new paradigm to merge different technologies and

[13] Health Sciences is not included in this list because it is mostly handled by the Human Health Sciences Research Ethics Committee (HSREC), however as the study will indicate, it is sometimes difficult to differentiate definite borders between the EBREC and HSREC domains and in many cases it overlaps. This challenge will be discussed in Chapter 3.

disciplines and combine various fields of study through collaboration and integration of approaches, making us rethink scientific research (Sharp *et al.,* 2011: 4). HEIs cover a significantly broad spectrum of research in Life Sciences, Physical Sciences and Engineering and strive to be aligned with the latest developments within the various disciplines. Institutions also explore and establish partnerships and collaborations with key government and industrial partners, which in South Africa include mining companies, Sasol, the Agricultural Research Council (ARC), Illovo and many more to address local needs and find solutions for the country and our continent.

HEIs also collaborate worldwide in research, on the one hand creating international partnerships and contributing to academic and scientific progress, but on the other hand at the same time contributing to a "blurring of national borders" that has far-reaching implications for research ethics, also in the field of EBR. Alejandro Adem from the University of British Colombia confirmed this point when he stated: "ideas transcend borders, no country controls the marketplace of ideas" (Owens, 2018). He noted that science is a global and international endeavour.

To understand the pluri-dimensionality and pluri-functionality of EBR in HEIs, I want to use a diagram called a "layer cake approach" (Fernandes & Guiomar, 2016: 517). It represents the multiple ecological interactions that need to be understood, considering different systems, spaces, processes and interactions, including ecological, socio-economic, cultural, biological, psychological or socio-ecological. It also shows the interdependence and interconnectivity between the systems and the role of humans and other life forms within these systems.

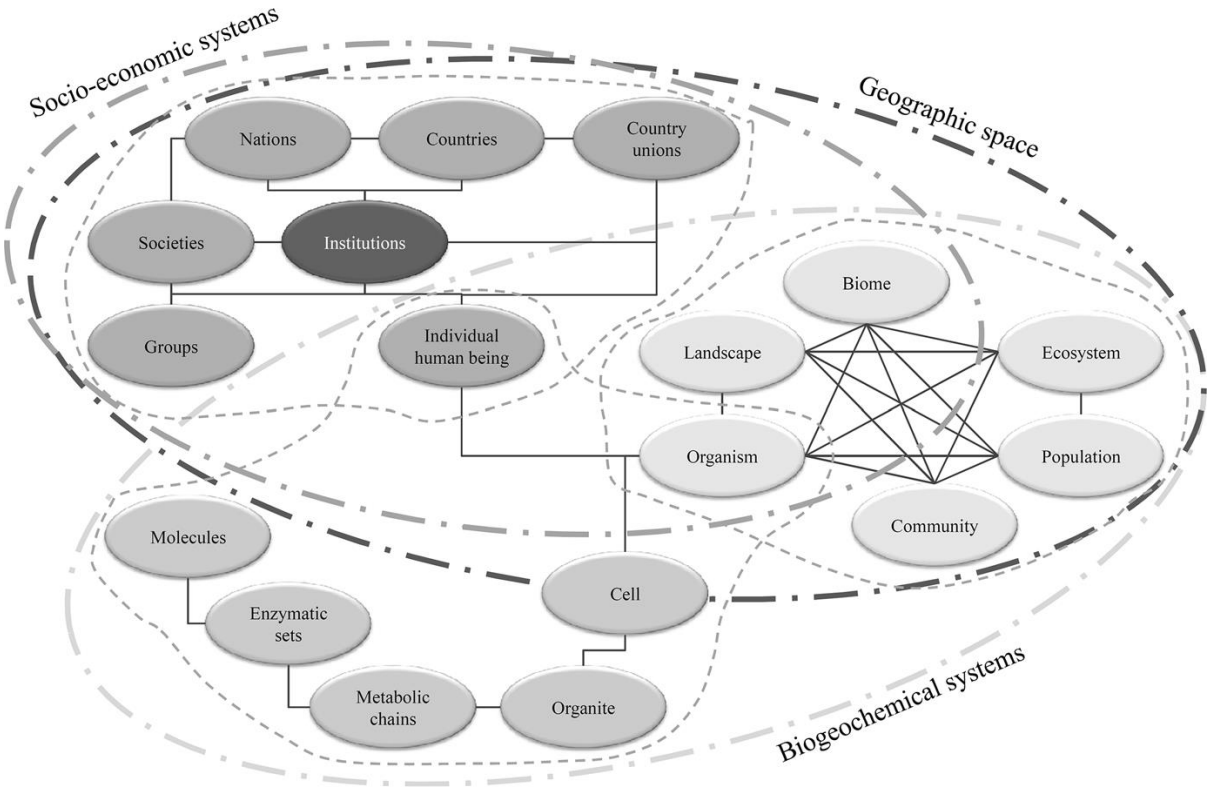

Figure 1: *Layers of the complex interactions between ecosystemic, individual and societal systems, as well as the derived or related biogeochemical and socio-economic systems, as well as the corresponding geographic space* (Source: Fernandes & Guiomar, 2016: 517)

With this complexity in mind and the broad spectrum of systems and interactions involved, the relevant EBR terms are discussed in the next section, followed by practical examples of research activities and related ethical concerns.

2.3.1 Overview of relevant terms in EBR

- **Biosafety and Bioethics**

Biosafety in a broad sense refers to the “safety of biological processes”. The narrower definition in the context of biotechnology is: “the containment principles, technologies and practices that are implemented to prevent unintentional exposure to biological agents and toxins, or their accidental release” (Kumar, 2015: 2). According to Article 1 of the Cartagena Protocol, biosafety can also entail the safe handling, transfer and use of living organisms modified through biotechnology (Secretariat of the Convention on Biological Diversity, 2000) It can also be explained as the policies and procedures adopted to ensure biotechnology's environmentally safe application. Biosafety is thus the effort to eliminate or reduce the risks of biotechnology and its products.

Laboratory biosafety is crucial to avoid infections due to bacteria, viruses, fungi, human cell lines, recombinant DNA, human blood or unfixed tissue, or to prevent accidental release into the environment. Occurrences such as these are called Laboratory Acquired Infections or Intoxications (LAIs), which include all infections that are acquired through laboratory activities, regardless of their clinical or subclinical manifestations. Therefore, strict biosafety guidelines need to be followed to reduce LAIs and under best case scenarios, strict guidelines are followed to ensure laboratory safety (following national and international guidelines, the most prominent of which are that of the WHO [2006]). It is a moot question, though, whether these guidelines are followed by all countries and all laboratories working with biohazardous materials and processes.

Crucial for EBRECs is that biosafety is related to many different fields of research, including, but not limited to the following examples:

- Medicine (e.g. viruses, organs or tissues from a biological origin, genetic therapy products, nanoproducts, all of which require different levels of laboratory containment protocols)
- Agriculture (e.g. reducing the risk of alien viral or transgenic genes, genetic engineering or prions, reducing the risk of bacterial contamination of food, plant breeding and weed science)
- Ecology (e.g. the importion of different life forms from beyond ecoregion borders)
- Molecular Biology (e.g. working with micro-organisms, blood and cell lines)
- Chemistry (e.g. working with hazardous chemicals and synthetic products)
- Synthetic biology (e.g. risks associated with some laboratory practices)

Biosafety covers a broad spectrum and includes environmental safety, food safety, human safety and socio-economic impacts. Therefore, it is an interdisciplinary field that provides for biological as well as material sciences (European Commission, 2013). Modern biotechnology, however, resulted in several biosafety issues such as the outbreak of infectious diseases, invasion of alien species or the escape of GMOs, threatening species diversity, societies and the ecological environment. The worldwide concern regarding biotechnology, genetic engineering and safety and risk management in these research fields, therefore, needs careful consideration by the EBREC. The purpose of this would be to help reduce exposure to potentially harmful agents emerging from laboratories to safeguard the environment as well as human and non-human life.

In Figure 3 below, an overview is given of biosafety needs and what needs to be considered in response to them by governments in general, but also by researchers and EBRECs.

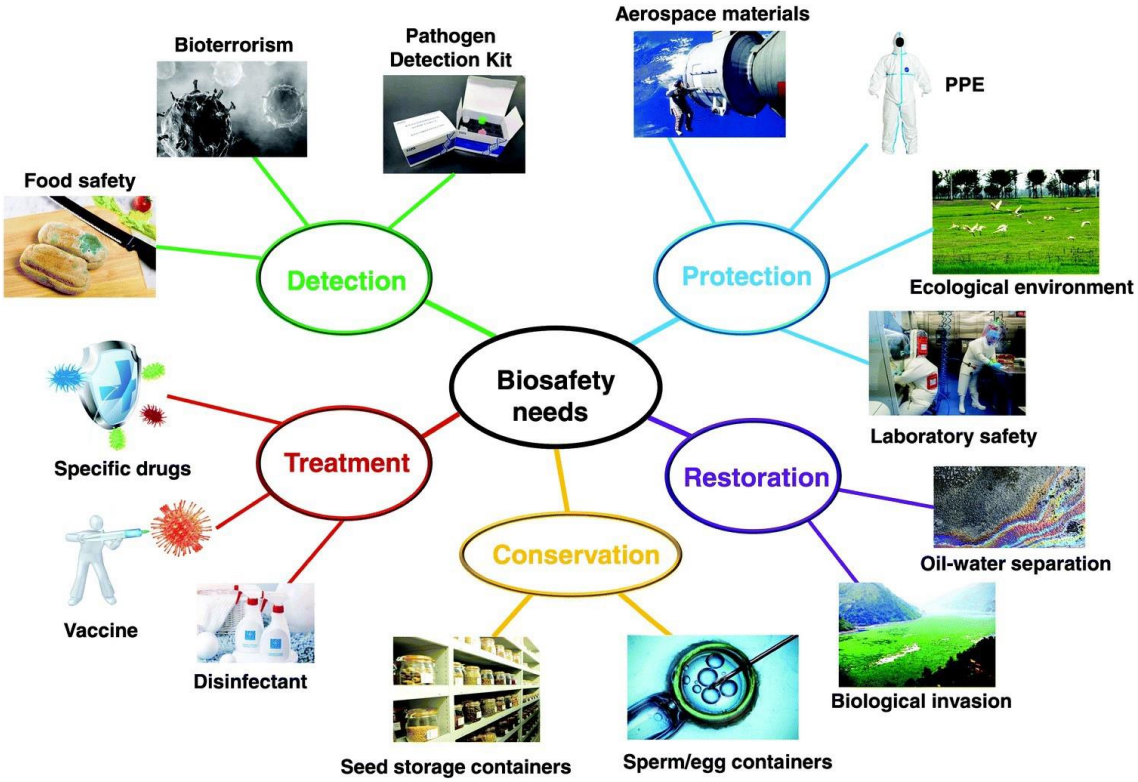

Figure 2: *Biosafety needs and their corresponding biosafety materials* (Source: Yingjie *et al.,* 2020: 1932)

New enhancements in biotechnology produce concerns about what is ethical or unethical. These questions fall in the realm of **bioethics**, a term first introduced in 1927 by Fritz Jahr from Germany (Gupta *et al.,* 2016: 508).

Fritz Jahr was a philosopher and educator in Halle an der Saale. He proposed a "Bioethical Imperative" built on Kant's moral imperative[14] but extended it to all forms of life. Unfortunately, due to morally and politically turbulent times, it had no immediate effect (Lopes, 2014: 256; Zagorac, 2011: 142)

In the 1970s, Shriver and Hellegers from Washington used the term "bioethics" with regard to medical dilemmas and ethical challenges due to new technologies in medicine. However, the literature indicates that Van Rensselaer Potter from Wisconsin is regarded as the person who revived the term in 1971 (Sateesh, 2008). In principle, Potter was concerned with the environment and the sustainability of human life on the planet. Potter expressed great concern in his publications, an article in 1970 and later in his book published in 1971, regarding the exponential growth of scientific knowledge without adequate consideration of the

[14] Kant's moral imperative: "Act as you would want all other people to act towards all other people. Act according to the maxim that you would wish all other rational people to follow, as if it were a universal law." (Pecorino, 2002)

consequences for the survival of life on Earth. He focused on the challenges imposed by new technologies and genetics.

Albert Jonsen points out that the neologism "bioethics" received canonical status in 1974 when the American Library of Congress catalogued it (Lopes, 2014: 256). The term gradually developed and incorporates moral issues in Life Sciences, Biology, Medicine, Environmental, population and Social Sciences (Sateesh, 2008).

Prof José Agosthinho Lopes considered the different neologisms of bioethics and then defined bioethics as:

> [...] a form of applied ethics that is concerned with solving problems related to life (bios). At the moment that human action gains the power to change life as if it is naturally given to us, this action on life falls within ethics – especially Bioethics (2014: 255).

In this broad sense, **bioethics** encompasses much of what we have already identified in this thesis as **environmental ethics**. For the purposes of my thesis, however, I will not use these two concepts interchangeably. Unless otherwise indicated, I will link **bioethics** with the ethical concerns related to biotechnology (as delineated above) and **environmental ethics** with ethical concerns having to do with the impact of research on the natural environment, ecosystems, biodiversity and the biosphere. This is of course not a definite distinction, but rather one with porous boundaries, explaining the consideration of these "two sets" of related and overlapping concerns in one body; here identified as the EBREC.

- **Biorisk, Biohazard and Biosecurity**

Biorisk "is the likelihood of the occurrence of serious infection due to exposure to pathogenic microorganisms or biohazards" (Gupta *et al.,* 2016: 505). Exposure may lead to severe infections, allergies or clinical problems and therefore need to be managed by risk assessment. Biorisk could also be related to environmental concerns in research activities, i.e. genetic engineering or genetic manipulation in animals, plants and micro-organisms.

Biorisks can only be managed if international policies, control systems and regulations are in place on many levels and contexts to ensure that only legitimate scientists/researchers can access potentially dangerous material and processes. In addition, procedures to oversee research projects that can have dual use,[15] i.e. used for good or hostile purposes, are also important in this regard. In fact, adequate measures in all the research areas are important to prevent adverse events due to biorisk, and again, this points to the crucial role that EBRECs

[15] "Dual use" in research will be discussed in more detail in Chapter 3.

can and must play in the assessment of research before commencing. This is all the more important and complex because biorisk could be unforeseen, accidental, due to human error or bioterrorism threats (Parker, 2015: 2).

Laboratories provide a crucial space for research activities. **Biohazards** in the laboratory environment, meaning biological substances that pose a threat to living organisms or potentially dangerous pathogens, need to be contained and handled safely and securely to ensure biosecurity. Biohazardous materials include viruses and organisms that are infectious to humans, animals and plants. It also includes rDNA or synthetic DNA and other biologically active agents that can cause diseases or harm (i.e. venoms, toxins and allergens). Another dimension of the task of EBRECs is thus to help determine whether using biohazardous biological materials in research could expose risk to the environment, the researcher, participants or society.

The African Union defines **biosecurity** as "the protection, control and accountability for valuable biological materials within laboratories to prevent their unauthorised access, loss, theft, misuse, diversion or intentional release" (WHO, 2006: iii, 2). Biosecurity, however, is becoming more of a challenge, also for EBRECs, since intentional misbehaviour with the malicious use of pathogens or toxins to harm and threaten people or disrupt societies is becoming a global problem and reality (Kumar, 2015: 2).

Iqbal Parker from the University of Cape Town indicates that the existing legislation in South Africa to deal with biorisk and biosecurity, or to monitor these kinds of issues, is fragmented. (2015: 2) This unfortunate situation clearly puts extra responsibility on EBRECs. Parker also expresses his concern about a low level of awareness among South African researchers regarding national and international regulations, conventions and laws related to EBR and biosafety practices (2015: 2).

- **Bioprospecting and Biopiracy**

The exploration of biodiversity, as mentioned above, is called **bioprospecting**. A definition for bioprospecting is: "The exploration of biodiversity for commercially valuable genetic resources and biochemicals" (Reid *et al.,* 1993; Christoffersen & Mathur, 2005: 254). The use of biological resources for commercial and industrial purposes hold promise for new developments and better consumer goods, energy and environmental benefits. It is all about exploring nature to improve the quality of life. Hence the exploitation of natural resources holds ethical, cultural and technological challenges that will be investigated in more detail in later sections.

Biopiracy, in contrast to bioprospecting, entails the illegal use of traditional knowledge, usually about the medicinal or related properties of biological entities, without permission or when a culture group is exploited. Biopiracy is defined as “the appropriation of the knowledge and genetic resources of farming and indigenous communities by individuals or institutions seeking exclusive monopoly control (usually patents or plant breeders' rights) over these resources and knowledge” (ETC Group Communique, 2002: 1) The Nagoya Protocol is the first international instrument that acknowledged indigenous people's rights and prescribes legally binding international measures to control the exploitation and commercialisation of indigenous knowledge (Teran, 2016: 13) The Nagoya Protocol will be discussed in Chapter 4 together with its implications for research ethics.

- **Biotechnology**

There are many variations of definitions for the term **biotechnology**. The following explanation by Dr Ramazan Asmatulu was used at the American Society of Engineering (ASEE) Conference in 2015 and reads as follows: “[Biotechnology is] the study and manifestation of living bodies or their components (e.g., molecules, organs, cells, and tissues) in order to improve their living conditions” (2015: 1). He further indicates that synthetic biology can be seen as a sub-category of biotechnology, and is the “designing and combining of biologic molecules such as deoxyribonucleic acid (DNA), ribonucleic acid (RNA) and proteins in order to provide a better understanding of the biological phenomenon and produce biological systems with certain functions” (2015: 1).

Another, perhaps more practical definition of biotechnology comes from the Merriam Webster online dictionary: “the manipulation (as through genetic engineering) of living organisms or their components to produce useful and usually commercial products (such as pest-resistant crops, new bacterial strains, or novel pharmaceuticals)” (Merriam Webster, n.d.).

In brief, the Organization for Economic Co-operation and Development identified the following biotechnology techniques to list different kinds of research activities (Collins *et al.,* 2018: 40–41):

- **DNA/RNA:** This area includes genomics, gene probes, genetic engineering, pharmacogenomics, gene expression profiling, sequencing or synthesis amplification.
- **Cell and tissue culture engineering:** Particularly the engineering of cell/tissue culture or cellular fusion. Additionally, it includes vaccines or immune stimulants. This kind of engineering also includes breeding technologies and embryo manipulation.

- **Proteins and other molecules:** This area involves sequencing, synthesis or engineering peptides and proteins. It also covers protein isolation and purification as well as the identification of cell receptors.
- **Gene and RNA vectors:** Research with certain viruses include vectors to deliver a new gene by infecting the cell. With this, the viruses are modified to prevent certain diseases in people. With retroviruses, the genetic material integrates with a new gene into a chromosome in a human or an affected cell. Viral vectors for gene therapy use several types of viruses, such as retrovirus, adenovirus and herpes simplex virus, modified in a laboratory for gene therapy applications.
- **Process biotechnology techniques:** Biotechnology techniques such as biorefining and bioprocessing focus mainly on the bioconversion of renewable resources to chemicals and fuels to save fossil energy. Research in molecular aquaculture aims at better product quality and increasing production. Another process in biotechnology techniques is fermentation using bioreactors. The bioreactor is a container or system that maintains the biologically active environment. In other words, it is an apparatus or place to grow organisms such as bacteria or cells under controlled conditions.
- **Nanobiotechnology:** is a multidisciplinary research field where nano- or microfabrication processes may be utilised to build devices for biosystem studies and drug delivery applications.
- **Bioinformatics:** combines computer science, information engineering, mathematics and statistics with biology to interpret biological data. An example is database construction for genomes and protein sequences.
  (Collins *et al.,* 2018: 40–41).

With modern biotechnology, at best researchers strive to combat debilitating diseases, to fuel and feed the world, use cleaner and less energy, ensure more efficient industrial processes, to reduce our environmental footprint and many more ways to heal and empower the world. (Convention on Biological Diversity of 1992: Article 2) With this in mind, biotechnology can be divided into five branches: human, environment, industrial, animal and plant, and its applications are grouped into different research areas that are colour coded[16] for ease of reference: Red, Green, White, Grey, Yellow, Blue, Gold, Brown, Black, Orange and Violet Biotechnology. This will be explained and discussed with examples in section 2.3.2.

[16] Dr Rita R Colwell introduced these categories in 2003. The different colour codes will be explained and discussed in the next section with relevant examples.

Color Type	Area of Biotech Activities
Red	Health, Medical, Diagnostics
Yellow	Food Biotechnology, Nutrition Science
Blue	Aquaculture, Coastal and Marine Biotech
Green	Agricultural, Environmental Biotechnology – Biofuels, Biofertilizers, Bioremediation, Geomicrobiology
Brown	Arid Zone and Desert Biotechnology
Dark	Bioterrorism, Biowarfare, Biocrimes, Anticrop warfare
Purple	Patents, Publications, Inventions, IPRs
White	Gene-based Bioindustries
Gold	Bioinformatics, Nanobiotechnology
Grey	Classical Fermentation and Bioprocess Technology

Figure 3: *Colour coding of biotechnology categories* (Source: DaSilva, 2004)

Thus, biotechnology cuts across a wide range of research areas, is intimately tied to scientific knowledge and human interests, and therefore is inextricably linked to ethics, i.e. in all of its forms, biotechnology entails a value-driven alteration of life, shaping it into different forms. However, the genetic engineering of living cells is but one aspect of this, and it seems to be continuously immersed in controversy as different ethical concerns and dilemmas are brought to bear on it.

Saurabh Bhatia explains that intentional modification and genetic manipulation of the natural world have been used for centuries to modify plants and animals to improve food production for human needs and also in farming for selective breeding and fertilisation. Fermentation techniques are a simple everyday process to transform milk into cheese, or grains into beer or bread. New biotechnology processes, however, enabled the ability to alter many life-forms by extracting and transferring strands of DNA and genes, manipulating the intricate genetic structure resulting in living modified organisms (LMOs) or genetically modified organisms (GMOs) (CBD & UNEP, 2003: 4).

The modification of food and animals is now generally used in many ways, e.g., enhancing sustainable food production, pesticides, vaccines, new industrial products and better fuels. Kofi Annan, the UN secretary, however, sounded this warning, underlining the rationale for

ethically sound research in this area: “Biotechnology could contribute significantly to the achievement of the objectives of the Convention on Biological Diversity and the attainment of the Millennium Development Goals. However, it must be developed judiciously and used with adequate and transparent safety measures” (2003: 15).

With this background in mind and a better understanding of the applicable terms and explanations, the next section will explain the different types of biotechnology followed by some relevant examples.

2.3.2 The types of biotechnology

As per the overview given in section 2.3.1 above, biotechnology can be divided into a variety of colours such as blue, red, green, violet, etc. These colours will be defined and explained below.

- **Red biotechnology.** According to the Biotechnology Innovation Organization (BIO), this entails the health or medical branch of biotechnology, responsible for utilising organisms to produce drugs such as antibiotics, vaccines or regenerative therapies, like using stem cells for the treatment of injured tissue or the production of artificial organs.

- **Green biotechnology.** This applies to agricultural processes or plant biotechnology including genetically modified organisms, transgenic plants and bioreactors. It is further used for pest resistance and strengthening crops against microorganisms and extreme weather conditions, such as frost or severe droughts. It thus includes various applications of plants and photosynthetic organisms and for many industrial purposes with the aim to generate products such as biofuels, paper, textiles, pharmaceutical substances and improved crops.

- **Grey biotechnology.** This type of biotechnology refers to ecological or environmental applications. The purpose is for restoration and focuses on the maintenance of biodiversity. It is all about removing contaminants or contaminated natural ecosystems such as soil or polluting gases, purification of water, eliminating hydrocarbons and heavy metals that damage the biosphere and pollutants. An example is plastic-eating bacteria. Grey biotechnology uses living organisms such as fungi and algae and classical fermentation to decay pollution material and convert it into more useful forms.

- **Brown biotechnology.** This kind of technology concentrates on the desert and arid soils. It is also called Desert or Arid Zone Biotechnology. One of the aims is to develop disease-free high-quality enhanced seeds for arid soil and extreme environmental conditions.

- **White biotechnology.** This technology focuses on the production of low resource-consuming processes and products. It is also called Industrial Biotechnology. Examples are gene-based bioindustries for industrial advances and procedures as well as the improvement of manufacturing processes, biofuels, chemicals and other technologies such as biodegradable plastics. Another example is sweeteners with zero calories.

- **Yellow biotechnology.** This refers to Food Biotechnology that focuses on food production and nutrition science. For example, it includes research to reduce the levels of saturated fats in cooking oils.

- **Blue biotechnology.** It is related to seas and ocean, marine resources and aquatic environments to control harmful water-borne organisms. It is called Marine Biotechnology and can be used to obtain biofuels from microalgae. Another example is wound dressing coated with a kind of sugar derived from crab and shrimp shells.

- **Gold biotechnology.** It is a technology that is used for everything related to bioinformatics, hardware and software for data analysis of biological processes. It is responsible for obtaining, storing, analysing and separating biological information, e.g. sequencing of peptides, DNA alterations and amino acid sequences, nanotechnology and forensic investigation of crime.

- **Black biotechnology.** This dark biotechnology is all about biological wars and biocriminolgy. It investigates pathogenic, virulent and resistant microorganisms for converting into biological weapons or counteracting their harmful effects. An example is the bacteria *Bacillus anthracis* or *Coxiella burneti* that can cause fatal illnesses to the lungs. Another infamous example is the 2001 anthrax attacks in the USA.[17]

[17] The anthrax attacks in the USA happened seven days after September, 11 terrorist attacks in 2001. Letters laced with deadly anthrax spores were anonymously sent to media companies and congressional offices. Five people died and seventeen others were infected. The source was traced back to the government's biodefense lab of the scientist, Bruce Edwards Ivins. He committed suicide before facing charges. (National Center for Biotechnology Information [NCBI], n.d.)

- **Orange biotechnology**. This is the learning and teaching area in biotechnology with its strength in universities across the world. The knowledge it provides and its interdisciplinary integration converts it into a technology destined to offer goods and services and satisfy our future needs**.**

- **Violet biotechnology.** It is the part that handles the compliance, ethical and philosophical issues regarding biotechnology. It deals with applicable laws and the legal aspects surrounding science. It includes moral and ethical principles regarding topics such as germline manipulation, animal testing, cloning and assisted reproduction. It covers the legal aspects surrounding different kinds of EBR. It is also related to patents, publications, intellectual property and inventions and devoted to solving problems and regulate scientific actions. It is thus the governance of biotechnology through regulation and problem-solving.

With this background in mind and a better understanding of the applicable terms and explanations, I will now dig into practical examples of research activities of HEIs that fall within the ambit of EBRECs and indicate the ethical concerns they raise concerning EBR in action.

2.3.3 Research activities in EBR with practical biotechnology examples and ethical concerns[18]

The significance of research at HEIs is driven mainly by the social and economic needs of society and subsequently, research requirements in EBR constantly transform and expand. It is therefore also challenging to predict ramifications emerging from these developing research areas that give rise to ethical concerns: they often catch us by surprise as exciting new areas of "can do" confront us with new questions of "should we".

In this section, I will provide examples of research activities that typically fall within the ambit of EBRECs, and I will highlight possible concerns that may be associated with them. In this regard I will follow the grouping according to Dr Colwell's biotechnology colour coding for the different research areas. However, my aim is not to provide an exhaustive list of examples from these technological fields or to identify each and every ethical concern, I will rather provide a selection of examples and only point to the most prominent and vexing ethical concerns that will need to be considered by EBRECs in this domain. This will help us to better understand the nature and extent of the research fields constituting the domain of EBRECs

[18] Only five examples according to the various biotechnology colours are discussed in this section and it would be possible to elaborate on many other examples; however, these are covered extensively in the literature and can be consulted as required.

and deepen our insight into the ethical concerns with which they have to grapple. In this, a very concrete point of reference will be created by which the current principles used by RECs can be assessed in terms of the question whether they provide adequate guidance for the current and emerging challenges faced by EBRECs.

Example 1: Covid-19 research

Example 1 falls within the realm of red biotechnology and is a discussion on the relevant topic of the Covid-19 pandemic that was still raging at the time of writing this thesis. The Covid-19 pandemic has clearly shown that the world was poorly prepared to handle the pandemic's outbreak. It highlighted a concerning situation and the gaps in global biosafety and biosecurity practices.

Long before the outbreak of Covid-19, Thomas Frieden and his co-contributors (2014) warned against emerging pathogens, increased resistance to antibiotics and treatment, and possible infectious disease outbreaks and epidemics. Infectious agents are classified as bacteria, viruses, parasites, fungi, mites, prions and toxins, and the target of these infectious agents are humans, animals or plants. The same article mentioned that the intentional release of biological agents is a potential threat and that globalisation increases the risk. Frieden *et al.* state: “a disease is just a plane trip away, and an outbreak anywhere is a threat everywhere” (2014: 764). This prediction and warning in 2014 became a scary and global reality in 2020.

The WHO declared the coronavirus disease a health emergency and international concern in January 2020, and on 11 March 2020, the WHO characterised Covid-19 as a pandemic worldwide (Palayew *et al.,* 2020: 666). In South Africa, the first Covid-19 case was diagnosed on 5 March 2020 (RESCOP, 2020: 1). Researchers all over the world then started to work towards ground-breaking innovations to find ways to treat and prevent the virus. The situation's urgency led to new international scientific partnerships and multicentre, multinational Covid-19 research teams and projects were quickly formed.

Dr Sheetal Soni, a researcher from KwaZulu Natal, indicated in May 2020 that more than 90 vaccine trials had been undertaken worldwide by that time (Soni, 2020). It thus became clear that the usual timeframes for a research ethics review in the conventional format were drastically reduced. But the question is, will the expedited reviews and approvals not undermine critical ethical principles, and how do we safeguard scientific research integrity? Misconduct and fraud in research are relatively common phenomena, and the framework of crisis in which research on Covid-19 was, and is being done, creates ample opportunities for serious shortcuts to be taken. A case in point are two Covid-19 articles published in prestigious

medical journals that have recently been retracted due to fraudulent information.[19] In both cases, the extensive dataset raised scepticism, and the authors could not provide the full dataset (Boetto *et al.,* 2020: 2). This provokes moral, social, legal and safety issues. To illustrate the challenges, I will discuss some examples and related ethical concerns as they relate to "Red biotechnology" in general and Covid-19 research in particular.

In response to the kinds of challenges highlighted above, HEIs in South Africa formed an informal voluntary Research Ethics support group (RESCOP) including the chairs of RECs and other relevant research ethics role players. RESCOP supported the rapid review of Covid-19 research but emphasised that national and international norms and standards must always be adhered to (RESCOP meeting notes, 24 March 2020). The general consensus in this regard is that researchers cannot compromise scientific integrity and ethically sound research practices due to international emergencies and time constraints (WHO, 2020).

Most of the Covid-19 related research revolves around a cure, vaccine or ways to contain the virus. Researchers want to demystify the disease and understand the virus' transmissibility. It is a race against time to find solutions and potential vaccines or agents targeting the virus or host cell components. There is a tremendous need for virus-specific research. Attempts to speed up the process raise ethical and safety concerns, for example, researchers skip the animal testing part and immediately introduce it to humans (Kahn, 2020). Kahn discussed this issue during an international webinar organised by the Nuffield Council on Bioethics. It was indicated that this was done in China and the USA, raising ethical questions concerning risk and safety (Whittall, 2020). [20] On the other hand, Oxford University had a much more ambitious way of speeding up the process. They mass-produced the vaccine while still testing it (Frunza, 2020: 25). This meant if the vaccine proved to be successful, the gain would be enormous, but if unsuccessful, they would end up with millions of unusable vaccines that needed to be destroyed, causing not only a financial loss but quite a concerning ethical and environmental

[19] Expedited approvals also resulted in large volumes of expedited publications. In an article of Adam Palayew and others regarding pandemic publishing, they indicated an average time of 6 days from receiving the article to acceptance of the article – a process that can generally take roughly up to 100 days. Although the nature of the pandemic warrants accelerated publications, adequate steps to safeguard the integrity of research are crucial. The investigation shows thousands of Covid-19 journal articles are submitted weekly. It raises concerns about the quality of Covid-19 publications and the risk of misinformation and the lack of scientific integrity that can lead to risky or harmful consequences. Flawed publications will result in the mistrust of the public and poor policy decisions, causing an "infodemic" (Palayew *et al.,* 2020: 667; Boetto *et al.,* 2020; 1).

[20] Mia Rozenbaum asked the question if we can fight Covid-19 without animal testing? Animal testing is normally a critical step in vaccine or drug development. A new vaccine can take between 5–20 years of development before it is available. This is for safety reasons and to efficacy. The president and CEO of the International AIDS Vaccine Initiative indicates that given the current emergency that animal testing can be skipped. He stated: "I personally think that's not only appropriate, I think that's the only option we have" (Rozenbaum, 2020). While Arthur Caplan from the New York University's Grossman School of Medicine gives the following warning: "The more you speed it up… the greater the obligation you have to track what's going on when you get it out into the real world" (Caplan, 2020).

issue. Research ethical questions around this for EBRECs include: how will these vaccines be disposed of and where will they be discarded? What impact will it have on the environment and what will be the health risks? In this regard, the task of an EBREC will be to understand and approve the method of disposal and ensure effective waste disposal management within the framework of applicable legislation regarding biohazardous waste disposal.

Additional questions that EBRECs face in this regard revolve around biosafety issues when working with potentially dangerous viruses. "Gain-of-function research"[21] (to be discussed later in Chapter 3) poses ethical and biosafety concerns, as explained by Dr Talkmore Maruta and cited by Sandisiwe Shoba (2020): "…it can increase the pathogenicity or transmissibility of potential pandemic pathogens". It can also be hazardous to communities and frontline workers in cases of harmful mutations of the virus, as previous viral epidemics and related mutations showed, which led to well-known outbreaks such as HIV/AIDS, Ebola, SARS, Zika and many others (Shoba, 2020). Constant mutation of viruses and the threat of transmission remains a global concern (WHO, 2018: 19). These research areas thus create multiple safety concerns that could lead to valid ethical questions in the EBREC domain such as "Are the lab's safety measures sufficient to protect the research team, collaborators and the environment? Are the staff adequately trained in all the procedures to ensure a safe environment?" Clearly, EBRECs should stress the importance of adequate safety measures and the protection of research staff (Dhai, Msomi & McQuoid-Mason, 2008: 25).

While research to combat Covid-19 involves methods that fall within other "colour codes" of biotechnology as they were identified above, such as gene-editing, bio-informatics and nano-techniques, and while all of the innovations in these fields are linked to the general problem of regulatory frameworks and legislation not keeping up with the rapid advancements in biotechnology and bioscience (Shoba, 2020), these themes will not be investigated further within this sub-section. These aspects and the ethical concerns they raise will be referred to in the sub-sections that follow.

Example 2: CRISPR-edited mushroom and golden rice[22]

Research in biotechnology products increased rapidly in scope, scale and complexity, influencing all aspects of life. Exciting green biotechnology developments include research

[21] "Gain-of-function research" (GOFR) involves experiments that increase the transmissibility of pathogens (Selgelid, 2016: 923).

[22] The examples of CRISPR-edited mushroom and golden rice are two different processes, which raises the question of the difference in ethical issues related to transgenic versus gene-editing plants. To pursue this question in further detail, however, falls outside the scope of this thesis.

where plant varieties can act as bio-factories, enhancing food quality and nutritional value and boosting agricultural productivity. It can bring an end to malnutrition and food insecurity. However, according to the Mansfield Center at Montana University, agricultural biotechnology may have the following primary ethical concerns: 1) the spread of transgenes into the environment or gene flow; 2) the possible negative impact on non-target species; 3) possible pest resistance that can develop; 4) creation of superficial organisms; or 5) tempering God's creation of nature (Steiner, 2020: 22).

The first crops genetically engineered and approved in the USA were produced in the 1980s, first tobacco and then Calgene's Flavr tomato. The tomatoes were modified to include a DNA sequence that inhibited producing a natural tomato protein, increasing the firmness and extending the Flavr Savr variety's shelf life. In 2016 the US government approved the first genetically modified CRISPR-edited organism, a mushroom genetically modified with the gene-editing tool CRISPR–Cas9 and cultivated in a laboratory greenhouse setting to resist browning. A plant pathologist at the Pennsylvania State University engineered the CRISPR-edited mushroom (Waltz, 2016: 293).

The best known and most controversial example of genetically modified food, however, is Golden Rice. In 1999 professors Ingo Potrykus and Peter Beyer introduced their project to the Rockefeller Foundation. They genetically altered and biofortified rice crops to increase the nutritional value of these crops. The goal was to combat vitamin A deficiencies in developing countries. With biofortification, the nutritional value in crops is increased. It is genetically modified to produce beta carotene and the beta carotene is converted into Vitamin A when metabolised by the human body (Freese, 2001; Mayer, 2005: 726–727). Despite thorough research, many ethical and unanswered questions remain. According to the consequentialist ethical framework,[23] the first question is whether the benefits outweigh the risks? Will the planting of golden rice bring good or more harm?[24]

Risk is always the first ethical factor to consider with research in green biotechnology, which includes antibiotic resistance or potential allergies. An EBREC should therefore determine the possible negative consequences of planting or consuming golden rice or manipulating fresh food products. Another possible concern for EBRECs to consider is the potential effect of

[23] A consequentialist ethical framework is primarily concerned with "the ethical consequences of particular actions". It focuses on the future effects of an action considering how it will directly or indirectly affect a person or the environment. The consequentialist framework considers ethical conduct that will achieve good consequences or the best in a given situation (Brown University, n.d.).

[24] Golden rice is only mentioned here as an example, and while it has been around for a long time and has recently (2018) been approved for commercial release in the Philippines (and the US, Canada, Australia and New Zealand have declared it safe for consumption), it does not take away that its initial introduction raised numerous questions that would fall squarely within the ambit of an EBREC to explore (Alvarez, 2021).

cultivating golden rice or genetically modified mushrooms on the surrounding environment and the influence on biodiversity.[25] Furthermore, the socio-economic implications for developing countries will affect small-scale farmers if market dominance (from big companies) arises. Another crucial ethical factor is listening to the developing countries inhabitants' voices and letting them decide if they are prepared to plant, for instance, the golden rice crops (Tickel, 2014). In this regard, EBRECs cannot act upon opinions or media concerns, but need to make informed decisions and ensure safe research practices within a framework of balancing the aim of ensuring a safe environment for future generations with the more immediate needs of present generations [26]to secure and safeguard food supply integrity.

For example, The US Department of Agriculture reported a serious incident where food crops were contaminated by a crop designed and tested for pharmaceutical products. The crop was supposed to be destroyed after the testing, but the research team neglected to do so. Due to this inattentive action, the surrounded crop fields were pollinated and contaminated the year after the tests. This underlines the danger of drug-laced crops ending up on uninformed consumers' dinner tables and emphasises the ethical concerns with this kind of research and products (Cohen, 2002).

It is thus evident that while research in green biotechnology is vital for food production, the primary ethical consideration must be that the potential benefit must outweigh any possible negative impacts, biosafety issues or risk factors.

Example 3: Synthetic Artemisinin (chemical compound for malaria)

In this multidisciplinary area, which falls within the field of white biotechnology, ground-breaking research in South Africa involves developing synthetic Artemisinin, the main ingredient for anti-malaria drugs. Natural Artemisinin is derived from a Chinese shrub called sweet wormwood, and more than 70% of the world market is sourced from small farmers in Asia and Africa. However, the natural process is time-consuming and costly **(**Perron-Welch, 2019: 12).

The research team of the University of Pretoria discovered a new compound treatment for the elimination of malaria through the synthesis of Artemisinin (Reader *et al.,* 2021). Lyn-Marie Birkholtz, a professor in Biochemistry, was part of an international team and she explains: "the

[25] It is indicated that the CRISPR editing tool to alter an organism's genome is a less biologically disruptive way compared to traditional plant-breeding techniques but it is still considered genetic modification with the possibility of unintended alternations or mutations with possible risks to the environment and/or human health (Hall, 2016).

[26] There is a vast literature available on the question of intergenerational justice in the context of sustainable development and resource use. The articles by Barry (1997) and Spijkers (2018) provide value access points into this debate.

breakthrough involves the identification of unique compounds that are able to kill several stages of the malaria-causing parasite and can block the transmission of the parasite between humans and mosquitoes" (University of Pretoria, 2021).

Further to this, a South-African malaria parasite, *Plasmodium falciparum,* is transmitted to humans by female mosquitoes. The research team discovered new chemical compounds that killed the disease-causing form and blocked the parasite from infecting hosts. Dr James Duffy, Medicine for Malaria Venture (MMV) Project Director, describes the discovery as

> an important breakthrough that emphasises the potential to use existing drugs as inspiration for drug discovery projects targeting different diseases. Never before has this been more important than in light of current outbreaks, where the rapid response to discovering new chemicals able to kill infectious organisms is essential (University of Pretoria, 2021).

Currently, malaria causes more harm than any other parasitic disease. Vulnerability to malaria is generally due to social issues such as poverty, malnutrition and insufficient access to healthcare. Although widely acknowledged that malaria research for alternatives is crucial, ethical concerns always need careful consideration. It includes biosafety issues and the possible exposure to pathogens when observing the disease or during the development of research models of infection. The handling of dangerous biological material needs careful assessment due to safety issues.

Synthetic Artemisinin gives a cost-effective and viable alternative (Asveld *et al.,* 2019: 124). Nevertheless, an ethical concern could be that it undermines wormwood's agricultural production with dire consequences for small producers. It is not the task of an EBREC to block or prevent scientific innovation, but in cases like this, the task should be to inform and advise researchers of the social impact to enable them to minimise any negative impact it could have on the community. The possible benefits should be considered against the negative effect of SynBio regarding economic development. The question could be asked if the cheaper synthetic alternative could destabilise vulnerable economies when the income source for small farmers is in danger. The potential benefits measured against the possible adverse effects need to be assessed on a case-by-case basis. The USA Presidential Commission on Bioethics suggests that the principle of justice and fairness or economic and social justice should inform synthetic advancements (2019: 21). The commission also asked the following question "How for example, are we to measure and compare the benefits of a technological innovation that leads to an effective medical treatment available on an unprecedented scale at low cost

against the cost imposed by the disruption and displacement of previously existing technologies and the people whose livelihoods depend upon them?" (2019: 21).

Consultation before, during and after the research with potentially affected parties is therefore crucial and include local communities, national governments and international organisations (WHO, 2014). As indicated above, the involvement of the role-players is an ethical obligation. Indigenous people and communities should be part of the research initiative and included as beneficiaries in ventures to prevent resources and knowledge exploitation. An EBREC should thus not only consider the safety of laboratories and lab techniques, or potential ecological risks, but also as an equally important factor, questions of economic and social justice and the question whether researchers need and have acquired the consent of the community before any bioprospecting can start.

To summarise, Asveld, Osseweijer and Pasada from the Delft University of Technology claim that ethical issues in white biotechnology mostly centre around sustainability, social issues, economic and social justice (Asveld *et al.,* 2019: 121–122).

Example 4: Groundwater & Shale gas studies

This example is taken from the field of grey biotechnology. Researchers from the Institute for Groundwater Studies (IGS) at the University of the Free State (UFS), in partnership with independent specialists, have been appointed by the Petroleum Agency of South Africa (PASA) to design a groundwater monitoring network. The establishment and implementation of the Central Karoo network was to ensure and understand the baseline groundwater conditions. The aim is to cover an area of more than 180 000 square kilometres (De Lange & Bosman, 2020). The Council for Scientific and Industrial Research (CSIR) published a report in 2016 titled *Shale Gas Development in the Central Karoo: A Scientific Assessment of the Opportunities and Risks.* The report indicated and recommended that "a comprehensive understanding of groundwater conditions is required prior to the commencement of exploration to ensure proper interpretation of changes in groundwater over time" (Scholes *et al.,* 2016). Shale Gas development or "fracking" is intimately linked to water concerns and the impact of this development upon water resources.

A groundwater monitoring network must generate results and provide answers to all stakeholders, landowners and the government to assist in informed decision-making processes. In this regard, the ethical questions will determine the positive or negative outcomes for those who profit and those who bear the consequences. It is thus all about public acceptability and distributive justice as well as procedural justice and environmental justice

(Evensen, 2016: 3). Distributive justice means a fair distribution of benefits and burdens. Due to the negative publicity and the potential contamination of water, collaboration with the community to establish informed decisions and consent will be crucial. Procedural justice will concern the way water is used, transported or disposed. What will be the involuntary risks, in other words, exposure to risks without consent or even knowledge?

The ethical assessment of EBRECs in this particular kind of study should therefore cover community involvement and the participation of all stakeholders. The EBREC should investigate if informed consent regarding access to existing boreholes or drilling additional boreholes for other monitoring purposes is necessary, and if necessary, whether and how it will be acquired. Furthermore, it will have to consider the modes of communication regarding the results of the study: how will it be relayed to the landowners, authorities and all other stakeholders?

Example 5: Environmental knowledge system from indigenous SA cultures

This final example does not originate from orange biotechnology per se but is an excellent example of the inter-/cross- and multidisciplinary approach and connections of EBR. Ethical rules regarding indigenous knowledge will apply to this research. Two researchers from the University of the Free State, one from the Department of English and another from the Department of Zoology, examine environmental conservation in oral stories from indigenous South African cultures. This interdisciplinary research project is titled: *Environmentalism in South African oral cultures: An indigenous knowledge system approach.* The aim is to bring together cultural and environmental disciplines, investigating the relationship between indigenous knowledge and environmental awareness. The researchers will focus on isiZulu, Sesotho and Tsonga traditions. They seek to understand the history, consciousness and knowledge of African indigenous environmentalism before the advent of Western forms of conservation. It will include investigating how traditional societies consciously thought about environmental conservation, preserving plant and animal species and sustaining ecological balance (UFS, 2020). This is an example of a study that needs ethical clearance from more than one ethics committee.

In a study where different communities will be involved; the study design also needs to consider local traditions and cultural differences. The application to the EBREC must ensure that the proposed procedures are acceptable. Depending on the procedure's invasiveness, the challenge for the EBREC will be to ensure that the researcher is aware of the hierarchical structures within communities. Possible challenges for an EBREC are ensuring decolonising research processes in practice when working with indigenous information within communities.

The EBREC needs to recommend that the researchers adjust or abandon existing methods or invent new ones. It is important to acknowledge the indigenous communities' right to self-determination, ownership, acknowledgement of data and the power to define. Adding to these challenges is the lack of structures and guidelines for best research practices. It means the EBREC needs to be knowledgeable about best practices within the different communities. Site visits to investigate the indigenous environmentalism of the various cultural groups needs to happen according to the community rules and cultural directions.

2.4 Conclusion

In conclusion, we need to remember that there will be overlapping areas in EBR. In some cases, researchers need to apply with more than one ethics committee, e.g. Human EBREC and/or the Animal Ethics Committee. Some principles may overlap between the different committees, but the application of a principle could be very different. It will depend on the specific study and situation as briefly mentioned above with orange biotechnology. Examples such as these make it clear, therefore, that EBRECs do not only deal with non-human issues, but also with the correct procedures to inform stakeholders and communities about research that will involve or affect them, directly or indirectly, and appropriate processes to acquire their informed consent. The EBREC, therefore, need clear guidelines and principles to guide them in cases such as these. However, the crux is that participation of communities and all stakeholders is often complex, driven by politics and toxic power relations and this complexity is amplified when scientific advancements comes in conflict with the moral and social value systems of societies in which traditional and religious beliefs and rituals around resources often play a crucial role (Gupta *et al.,* 2016: 503; Dixit, 2003: 26) In this regard, the enormously difficult task of an EBREC would then be to help facilitate a balance between social values and biotechnological advances.

CHAPTER 3: SETTING THE SCENE FOR ENVIRONMENTAL AND BIOSAFETY RESEARCH ETHICS – II

3.1 Introduction

Given the background and examples discussed in Chapter 2, it is clear that the domain of the EBREC is a vast multidisciplinary field that raises multiple sensitive areas in environmental and biosafety research (EBR) that need careful consideration. In this chapter my aim is to delve deeper and more systematically into these sensitive areas and to sketch the challenges they pose for EBRECs. In Chapter 4, I will then be able to determine to what extent existing principles used by research ethics committees are adequate to resolve the challenges experienced by EBRECs. However, before I proceed with Chapter 3, it is necessary to first highlight the problem of positivist science that puts severe, but avoidable restrictions on our perception of the ethically sensitive questions raised by advances in biotechnology and other contemporary sciences.

3.2 The problem of positivist science

The positivist idea[27] that science and research are ethically neutral is long outdated (Matas, 2018: 257). The general consensus in the philosophy of science is that even in their constitution, science and research are not neutral but entirely value-laden (Matas, 2018: 257–258; Audi, 1982: 72). Indeed, it is conceded these days that even observation is not the neutral registration of facts by a passive observer; observation itself is driven by socially embedded values, of which “objectivity” and “universality” are two examples (Wagensberg, 2013: 331–336). Nevertheless, it should be borne in mind that research specifically is a social enterprise. In the conceptualisation of research questions, in the design of research, in the interaction with research subjects or objects and in the dissemination and use of research results, value choices with sometimes far-reaching ethical implications are involved in every step of the process (Matas, 2018: 258; Audi,1982: 72, 75). Therefore, the multicultural and social environment within which research is conducted and ethical concerns unfold, will determine how an EBREC must deal with it. The broader issues that frame the sensitive areas that I will discuss below include socio-economic issues, cultural issues, environmental issues, moral or religious issues, legal issues, safety or risk issues and health issues.

[27] A general discussion and early critique of positivist science can be found in *The Logic of Scientific Discovery (*Popper, 1959). This work was described as a stimulating discussion of scientific knowledge. Other insightful discussions regarding scientific positivism and research ethics is provided by Seth Abrutyn and Richard H. Brown (Brown, 1998; Abrutyn, 2019).

Mohammad Rashid from Maryland University believes that the ethics of biotechnology entails reflection on the underlying cultural and social conditions that form part of it and the immediate consequences of its use (Rashid *et al.,* 2015: 49). While remarkable success with EBR is evident and the potential to provide economic and other benefits is apparent, public resistance and discomfort with certain biotechnologies and innovations have increased (ibid: 2015: 50). Certain biotechnological techniques, such as gene therapy, human genome or cell technology, raise ethical and legal issues. Research in these areas will thus always be controversial because it can violate traditional, moral, ethical and religious values. Manipulating life through certain debatable techniques (that may not be controversial to scientists at first glance) might create huge controversy and concerns and generate resistance from traditional, religious and cultural groups.

The same arguments apply to environmental advancements with examples such as biological pesticides rather than chemical pesticides. Such advancements could be valuable for the environment if safety could be guaranteed. The counterargument is that genetically engineered plants can reduce the need for fertilisers and therefore minimise the pesticide pollution of our valuable water resources. Nevertheless, it still raises concern regarding the capability of a GMO to escape and potentially introduce the engineered genes into other populations and non-target organisms such as non-pest insects (WHO, 2021). Inappropriate applications and the possible risk factors always need to be considered.

One of the first research advancements with genetic engineering in micro-organisms was the ability of bacteria to digest oil spills in the ocean (Rashid *et al.,* 2015: 50). While the primary aim of environmental biotechnology research is improving the environment, clearly releasing such organisms “in the wild” with the best of intentions and benefits in mind, raises negative public responses and concerns that must be investigated and addressed by the EBREC. Another concern, as already discussed in the examples in Chapter 2, is the possible consequences for developing countries with the potential impacts on socio-economic welfare and the effect on traditional cultures. The lack of relevant legislation, especially in developing countries, affects vulnerable societies and environments. Western countries, on the other hand, have the ability to regulate controversial actions and techniques by law.

Having said this in general terms, I now want to highlight and discuss the following sensitive research areas applicable to EBR in HEIs: 1) Research involving Genetic Engineering: Genome Editing, GMOs, CRISPR and Nanotechnology; 2) Research involving stem cells; 3) Gain-of-function (GOF) research; 4) Infected or invasive species and biological toxins; 5) Dual-use research; 6) Indigenous knowledge and patent rights and 7) Ethics dumping.

3.3 Ethically sensitive areas in environmental and biosafety research

3.3.1 Genetic Engineering: Genome Editing, GMOs, CRISPR and Nanotechnology

Genetic engineering comprises many different techniques for the manipulation of genetic material. It is a susceptible area that needs responsible, ethical conduct. Recombinant DNA (rDNA) or genetic material from different biological species can be modified to form new combinations of heritable genetic material. A preferred gene is removed from one organism and introduced to another, basically cutting and pasting the genetic material to create a targeted change in a plant or animal. It is also called “genome editing”. Organisms where the genetic material was altered to create novel traits in animals, plants, bacteria or fungi, are called genetically modified organisms (GMOs) (Rosenberg, 2017: 81–93). [28]

New CRISPR/Cas9 technology takes the process a step further by cutting and pasting genetic material of the same species while applying this technology to “germ cells” (sperm and eggs or embryos) changes the germline, and these genetic changes will pass on to future generations (National Center for Biotechnology Information, n.d.)

Johannes Rath (as cited in Schroeder, 2018: 107) posited that the conversion of a gene within a genome location could cause indistinguishable changes from natural mutations, which explains the argument that genetic modification is improper tampering with nature, and that the product or outcome is unnatural because it changes and interferes with the “essence of species” (Weale, 2010: 584). Thus, while genetic modification may have significant benefits, it also raises notable ethical concerns. Accordingly, and to put it bluntly, an EBREC also has a responsibility in the widest sense of the word towards poor or developing communities when they make an ethical decision on the social and economic benefits of research conducted within these communities or impacting these communities (even if the research is conducted elsewhere).

The numerous benefits of genetic engineering are evident. Genome editing is already used in cancer treatment, infectious diseases to create novel pathogenic organisms, environmental engineering and agriculture. Some essential agriculture applications are to modify insects, plants and micro-organisms to assist in better farming practices. Genetically modified crops

[28] GMOs are getting more and more important in order to improve conditions prevalent in the environment and to meet increasing demands. An ethics review should consider the post-release impacts of GMOs to ensure preventative and precautionary measures. This will be based on risk management and risk assessment. Methods should be monitored to control the negative health and environmental impact. The EBREC review should therefore ensure that research is in line with international biosafety regulatory frameworks to protect against ascertainable risks and to ensure proper risk assessment and the application of a precautionary approach. The review should include capturing the benefit, minimising the risks and ensuring quality of the final product. Review questions could include: What do the GMOs contain? Is it safe? How were the GMOs made?

are examples of exciting technology that can increase the nutritional value of food. The use of pesticides and insecticides can be reduced and vaccines are being produced. Unfortunately, fascinating developments like these can also cause unknown and unseen effects on ecosystems and the health of humans, animals and plants; for example, the insertion of an unrelated gene can induce allergies. The following is an example of such an unforeseen risk. A Brazil nut gene is transferred to a new soybean variety to improve the nutritional quality of soybeans. Unfortunately, consumers with nut allergies may be unaware of the nut gene, leading to adverse reactions (Gupta *et al.,* 2016: 513; Callaway, 2016:16). The high possibility of an allergen being transferred into other foods through genetic engineering can thus have serious health-related risks, all of which are factors that should be seriously considered by EBRECs when reviewing research protocols.

Wider social, economic and political factors can also play a crucial role in the global acceptance of sensitive technology. Religious beliefs, for example, can determine whether a technology is considered unethical in a certain cultural or societal context. To illustrate, for Muslims, any GM food must meet the halal criterion, which means that GM food with DNA from pigs would not be permissible for them (Jogdand, 2015: 53). Therefore, the EBREC in its decision-making processes should always be aware of and senstitive to any possible religious issues that can influence the conduct of research or the acceptability of its outcomes.

Additionally, while genetic engineering directly manipulates genomes in biotechnology, nanotechnology is manipulation on an anatomic or molecular scale. But in contrast with the gene-editing processes discussed above, nanotechnology uses synthetic and inorganic materials, less than 100nm in size (Florczyk, 2007). Nanotechnology is applied in various areas such as biology, chemistry and physics. The potential to create new materials with nanotechnology is applicable in medicine, engineering, environmental, energy, information and communication science with the possibility to provide solutions to global challenges. The same ethical issues mentioned for other technologies also apply to nanotechnology. So, again, while nanotechnology may have huge benefits for humanity, for instance in the treatment of diseases or certain disabilities, it also raises a whole suite of ethical questions around eugenics that need to be carefully considered by EBRECs in their review processes. [29]

In addition, the EBREC will also have to consider the impact of nanoparticles on the environment. Forczyk (2007: 278) indicates that the immense range of applications will make

[29] It is important to understand that the scope of responsibility of EBRECs is not well defined and the ethical complexities faced by these committees can put them in difficult situations. Examples mentioned may be considered outside the scope of an EBREC but higher education institutions are involved in research projects that may have a major impact globally, not only on the fiscal environment but also the social environment. I will argue that there will be borderline cases and uncertainties to determine how far the EBRECs responsibilities stretch. This is however a question for another study and falls outside the scope of this study.

worldwide regulations and governance challenging because nanomaterials are already part of the mainstream lives of consumers, for example, in things such as computers, sports equipment and sunscreen. However, because nanoparticles differ from everyday counterparts, the adverse effects cannot be derived from known macro-sized material toxicity and therefore it poses health and environmentally related safety risks. In this regard, Michael Berger importantly raises the concern that there is not enough data available regarding the undesirable effects of nanoparticles on the environment, and that it is thus still unclear if nanoparticles will create a new class of pollutants that is non-biodegradable (Berger, 2007). For EBRECs, the biosafety issues regarding nanomaterial thus requires special consideration. The two main areas relevant in this regard are:

1. The danger of free form nanoparticles and their possible release in water or the air during production, or as a waste product, which means that it can then accumulate in water, plant life or soil, and therefore can also ultimately affect animal and human health.[30]
2. In a fixed form as part of a product, nanoparticles will ultimately be recycled or disposed of as waste, which can create the same problems of ecological accumulation referred to above.

In this regard, the EBREC should thus not only be thoroughly informed about the biosafety aspects of nanoparticles, but also its disposal as waste, in order to ensure less contamination of nature (Berger, 2007).

In conclusion then, transgenesis or transgenic engineering and related research areas such as nanotechnology can be complex, controversial and do not always prove to be socially or ecologically efficient. Furthermore, genetic or human alterations and enhancements need to be carefully considered by EBRECs before any research in this area can proceed due to the many unforeseen implications and ethical questions that it raises (Gupta *et al.*, 2016: 511). But, on the other hand, EBRECs should also carefully consider and weigh the benefits that this kind of research may bring.

3.3.2 Stem cell research

Stem cell research is another sensitive research area that clearly falls within the domain of EBRECs. This kind of research is important for understanding the evolutionary development and differentiation of humans as well as the basic mechanisms involved. It also gives hope for new treatments of spinal cord injuries, diabetes and many other diseases. The capacity of cells to differentiate in all kinds of cells is a potential cure for many diseases. However, some

[30] Similar to the accumulation of DDT in ecosystems but nanoparticles will do this on a different scale.

ethical and political controversies in the different stem cell research areas should be considered here. Not all stem cell research will fall under an EBREC. The Health Sciences Research Ethics Committee will cover some stem cell research. However, due to the many multidisciplinary areas in research, EBRECs need to take note of some crucial areas of overlap. A precise line or differentiation between the responsible ethics committees, however, is not always possible because of the interdisciplinary nature of stem cell research. In some cases, both ethics committees will be involved.

Stem Cell research areas include: 1) Multipotent Stem Cells; 2) Embryonic Stem Cell Research: 3) Somatic Cell Nuclear Transfer; 4) Foetal Stem Cells and 5) Induced Pluripotent Stem Cells (Lo & Parham, 2009: 204).

According to Lo and Parham (2009), crucial ethical issues to consider in these research areas will be the handling and donating of biological materials. Informed and voluntary consent is clearly a vital consideration in this regard, when applicable. During the research process, further ethical issues to consider are the destruction of embryos or the creation of embryos specifically for research purposes. Some of the questions that will have to be considered by the EBREC in this context include the following: “Will payment to oocyte donors be necessary and appropriate, and if so, how should it be handled ethically?” Another ethical question will be determining the medical risks involved in oocyte retrieval and how the researcher will mitigate such risks (Lo & Parham, 2009: 205).

According to Lo and Parham, other considerations include using stem cell lines derived at another institution and ensuring that there are no conflicting legal and ethical standards when these stem cell lines are transported and/or moved across borders (2009: 205).

Multipotent Stem Cell Research is widely used and includes adult stem cells and cord blood stem cells. It does not raise particular ethical concerns other than the concerns mentioned above. Stem cells from cord blood can be banked and are widely used in research but cannot be expanded *in vitro* (meaning, used outside a living organism) (Lo & Parham, 2009: 204). Adult stem cells are more complicated, occur in many tissues and differentiate into other specialised cells. They are used to treat haematological malignancies or in cancer chemotherapy to modify the side effects. The more complicated the process of research in these areas are, the more critical the mitigation of all possible risk factors, of course, are. As such, this observation points to some of the questions that need to be asked about the composition of EBRECs: Is the expertise required to assess the integrity and risks of stem cell research present in, or available to the EBREC, and does the decision-making processes within the EBREC allow for the due consideration of such expert advice?

Embryonic Stem Cell Research is ethically and politically controversial because it involves the destruction of early embryos to obtain stem cells. The moral status of an embryo is a complex and controversial issue. Most people consider research with an embryo unnecessary, immoral and illegal. The ethical question is whether a fertilised egg can be regarded as a human being. In contrast, embryonic stem cells offer hope to many therapies and treatments for devastating diseases, giving another human hope for a new life (Jogdand, 2015: 43–46). Therefore, frozen embryos donated for research purposes after infertility treatment may be more acceptable, but still raise ethical questions. Some arguments are that life begins in the womb and not a refrigerator, therefore the morality of using embryos that would usually be discarded to improve or save lives, can ethically be justified (Lo & Parham, 2009: 205). However, the ethical concerns when a frozen embryo is donated include informed consent from the donors and ensuring the confidentiality of donor information. Due to the controversy with this kind of research, informed consent to use the embryo for research purposes is extremely important (ibid: 2009: 206). Waiver of consent is only applicable for the research use of de-identified biological materials that cannot be linked to donors. Examples will be cases of embryos that fail to develop sufficiently for implant purposes and are usually discarded. These materials can be de-identified to be used by researchers. However, the ethical justification for doing research without consent will be challenging to motivate, even if it is de-identified. Indeed, confidentiality of donor information will be a primary consideration for EBRECs reviewing protocols on embryo research.

Foetal Stem Cells can be derived after abortion from the foetal tissue to get pluripotent stem cells. However, abortion is already a controversial issue and, therefore, an ethical concern in this regard. On the one hand, some believe that abortion is permissible because a foetus does not have moral standing and therefore, the use of stem cells derived from foetal tissue does not have any moral barriers or ethical concerns. On the other hand, is a strong opposition regarding abortion. The stem cells are used for regenerative medicine or disease modelling. Disease modelling is necessary to assist with treating many diseases and understanding the progression of diseases. The appeal is that procuring and using foetal material from induced abortions can be complicit with the abortion, and it is not possible to obtain consent for the use of foetal materials (Harman, 2007: 207).

Somatic Cell Nuclear Transfer (SCNT) is possible when stem cell lines match another person's nuclear DNA. It has several scientific advantages because a stem cell line matched to a specific individual offers easier stem cell transplantations. But the ethical concerns to consider are the objection to creating embryos with a research intention, using them for research, and then destroying it. The ethical question in this regard is: “Is this not a violation of respect for nascent human life?” The intentional creation of embryos for research purposes is the central

moral concern in this regard. In rebuttal, the counterargument can be that entities created through somatic cell nuclear transfer are ethically and biologically distinct from embryos, and therefore, should pose less of a problem (Lo & Parham, 2009: 208).

This kind of research, however, makes cloning possible, e.g. Dolly the sheep, produced through reprogramming, meaning transferring nuclear DNA from a donor cell into an oocyte where the nucleus has been removed. However, cloning is very controversial, considered morally wrong and illegal in many states, and is a complicated ethical issue.

The cloning issue links to another ethical concern regarding the use of animal oocytes to create SCNT due to the shortage of human oocytes for research purposes (Sugarman, 2008). A major ethical concern is crossing species boundaries between humans and animals, and the possibility of transferring retroviruses or zoonotic diseases during the procedure (Bourret, 2016: 5).

An EBREC or any other ethics committee needs to address these concerns through strict oversight, as indicated by Lo and Parham (2009). They suggest the following guideline and examples: 1) prohibiting reproductive uses of embryos; and 2) limiting in vitro development. They also indicate that it is important to consider public repugnance, but they qualify this claim by saying it should not guide ethical judgments because public views can change over time (Lo & Parham, 2009: 209).

Induced Pluripotent Stem Cells (iPSCs) are derived by inserting genes using retroviral vectors. This technology can be employed for disease modelling and gene therapy in various diseases or regenerative medicine .This is a gateway for research in therapeutics and in studies regarding the molecular mechanisms of diseases, such as Parkinson's Disease, in an attempt to develop putative treatments for these kinds of diseases. It can also be used to produce cells for transplants in the case of injury or tissue degeneration due to certain disease conditions or cell replacement therapy. The primary advantage is that it can be created from the same patient who will receive the transplant. They are artificial stem cells produced from somatic cells, but they can proliferate and self-renew indefinitely, similar to embryonic stem cells. iPSCs can also be used in the evaluation of toxicity of chemical compounds, hazardous chemicals or pharmaceutical drugs (Singh *et al.,* 2015: 4).

This kind of stem cell research is considered ethically more acceptable because it is non-invasive with fewer concerns and risk factors than the previously discussed stem cell research procedures. Researchers use adenovirus vectors rather than retrovirus vectors to minimise the risks and eliminate safety concerns (Lo & Parham, 2009: 209). However, extreme scenarios cause concerns, such as to cross gametes. Fears are raised that these artificial

cells could conceivably be induced to infinitely versatile cells to form eggs or sperm. It is also a requirement that a donor needs to give consent for the use and testing of his sample and the collection of the sample should be carried out in an ethical way (Singh *et al.,* 2015: 14).

From this vantage point it should be stated that EBRECs clearly have the task to carefully consider the ethical challenges of the different areas of stem cell research insofar as they fall within the domain of the committee. But the task is not only to adequately discuss and assess the relevant ethical issues in their review, but also to reach recommendations that will not suddenly put a stop to stem cell research, but rather ensure that it is carried out in an ethically appropriate manner.

3.3.3 Gain-of-function (GOF)

Gain-of-function (GOF) experiments are mostly applied in virology to understand the biological mechanisms behind virus replication and transmission and is therefore regarded as a research area falling within the domain of the EBREC. GOF research is done when an organism's genome is changed, resulting in the acquisition of new or enhanced biological phenotypes. Concerns regarding GOF emerge when a gene's protein becomes overactive due to mutation and results in potential pandemic pathogens (PPPs). Examples of such PPPs are the coronaviruses (CoV), Severe Acute Respiratory Syndrome (SARS) and pandemic strains of influenza.

GOF methods include genetic mutations, gene insertion and synthesis. Synthesis happens when a new, improved function is created by combining two or more components to produce a new entity. Historical examples of these GOF research methods that raised ethical concerns are: 1) the development of the deadly strain of the mousepox virus[31], 2) the search for the 1918 Spanish flu virus[32] and 3) human synthesis of the poliovirus.[33].

Debra Mathews from Johns Hopkins University indicates that most ethical issues in GOF research revolve around the risk/benefit analysis (Mathews, 2021: V5). Pathogens can be highly transmissible, thus there is the risk of an uncontrollable spread in human, animal or

[31] Australian researchers inadvertently developed a lethal mouse virus. They used standard genetic engineering techniques to insert a gene into the mousepox virus hoping the altered virus would induce infertility in mice. Mice are a major pest in Australia and the idea was that this altered virus would serve as an infectious contraceptive for pest control. They discovered that the altered virus could kill even the naturally resistant and vaccinated mice. The findings were published but critics complained that the publication provided explicit instructions for terrorists who could use these techniques for the wrong reasons and dual-use purposes (Selgelid & Weir, 2010: 18).

[32] The H1N1 flu virus of 1918 caused a major pandemic. In 2005 an expert group of researchers searched the virus, sequenced its genome and recreated the virus in a safe and regulated laboratory setting in an attempt to understand and to prepare for similar future pandemics (Jordan, 2019).

[33] In 2002 the global media reported that researchers created a polio virus in a test tube. The research was condemned as irresponsible and dangerous but also hailed as a milestone in GOF research. It created a new reality of synthetic viruses (Wimmer, 2006: S3).

plant populations (Evans *et al.,* 2015: 901). However, Dr Thomas Briese explains that GOF research is a "proactive approach" to understanding what will or can happen in nature. In other words, GOF experiments are necessary to understand the ecology, biology and pathogenesis of viruses. For example, GOF research on CoV is necessary, even critical, for the development of vaccines (NCBI, 2015). During a Symposium regarding the risks and benefits of Gain-of-function Research, Subbararo emphasised that there is a need to develop new antiviral drugs. He stated: "Ultimately, GoF studies, which enhance viral yield and immunogenicity, are required for vaccine development" (Subbarao, 2015: 24).

But, the negative aspect is the risk of proliferation, meaning the reproduction or multiplication of pathogens through the rapid or excessive spread, which raises serious concern. The risk of an accidental release from a laboratory, spreading a virulent pathogen could lead to a global pandemic or an environmental disaster, as the Covid-19 pandemic clearly proved. Such a virulent pathogen is very likely to cause significant mortality (Mathews, 2021: V2).

The role of an EBREC in assisting researchers in selecting the appropriate Biosafety Level (BSL) is apparent when working with these pathogens and will depend on the biosafety and biosecurity risks of the study. Another risk factor that EBRECs need to consider in this regard is informational risks, meaning the need to determine what are, or will be, the risks of publishing and informing the world about Gain of Function research. In this regard, however, it is not only the institution of science that needs to be considered (in terms of the imperative to publish and share research results), but also the loss of public trust if people start to feel that they are not informed or even wilfully excluded from public debate. The picture starts to emerge that the task of an EBREC is an arduous one, taking its members on very treacherous terrain to negotiate, to say the least.

3.3.4 Biological toxins

Another research area that clearly falls within the ambit of the EBREC, is that of biologically active agents that can be defined as: "chemicals produced by living organisms that have toxic properties for another organism" (Janik *et al.,* 2019: 1). Toxins (some of which are also classified as venoms and allergens) are biomolecules and can be produced in many ways by fungi, bacteria, insects, plants and animals (ibid: 2019: 2). While scientific knowledge about toxins, venoms and allergens are extremely important in areas such as human, animal, plant and ecological health, unfortunately it is also the case that substances such as these can be used as potential biological weapons to cause disease or to harm other living organisms. It can also cause a negative impact on the environment or community. This emphasises the

need for EBRECs to monitor the use of biological toxins in research activities through strict biosafety measures.

3.3.5 Dual-use

Dual-use in scientific research refers to technology initially conducted for legitimate purposes to provide a potential benefit, which can then also be utilised to generate organisms, technologies, results, products or methodologies for harmful purposes. In other words, dual-use research can lead to misuse or malicious use of existing knowledge to cause harm (WHO, 2013). This kind of research poses a real threat and the possibility of serious consequences to national security, public health and safety, animals, the environment, agricultural crops or other plants.

Synthetic Biology can serve as an example in this regard, where researchers can construct organisms from scratch, with the dual-use concern that it could also be used for obscure reasons such as bioweapons. For example, the State University of New York announced in 2002 that they could synthesise a virulent and deadly poliovirus for the first time to create an organism entirely from “off-the-shelf materials” (Jogdand, 2015: 95). The research was widely criticised, but the researcher illustrated how easy it would be to construct bioweapons. The ability of researchers to construct artificial life forms with synthetic biology is a reality, highly sensitive, controversial and regarded by many as unethical. In 2010 the J. Craig Venter Institute created a single-cell, self-replicating organism as proof that genomes can be electronically designed, chemically made in a laboratory and then transplanted into a recipient to produce a self-replicating cell (2015: 95–96). This becomes a very scary capability if synthetic organisms are engineered to produce toxins and thereby create a biosecurity issue. However, Susan Wright, as cited in Miller and Selgelid, uses an interesting argument when she concludes that with an experiment that involves enhancing the virulence of a pathogen, the following should be considered: “[i]f there is no evidence of a threat posed by, say, a genetically engineered strain of cowpox that attacks the immune system, then there is no reasonable justification for developing such an organism. Arguably, to do so crosses the line between defence and offence” (2018: 35). Therefore, one of the important challenges for an EBREC is to promote ethical consideration and professional self-control among researchers through education and awareness-raising, and to assist in developing a culture of research integrity and responsibility (Salloch, 2018: 7).

Decision-making regarding the value and legitimacy of this kind of research that entails the risk of being misused for sinister purposes places considerable responsibility on an EBREC. The German Ethics Council did an analysis in 2014 regarding the empirical, ethical and legal issues related to dual-use in research (Salloch, 2018: 5). They emphasised in the analysis

that the ethics committee should be composed of experienced bioscientists, researchers, lawyers and an ethicist to deal with issues in their field of expertise. This range of competencies will be helpful to understand particular biological backgrounds and research practices of controversial experiments. They will also be able to assess compliance with legal regulations and deal with research ethics tasks, such as the protection of subjects or the environment and with risk-benefit analysis. However, Saloch warns that the ethics committee may not always be able to immediately classify a possible threat to security when reviewing the research (2018: 6). Saloch raises another concern in his article regarding the danger of conflict of interest for committees and researchers, meaning, on the one hand, to promote research and on the other, the responsibility to prevent misuse or harmful science (2018:6). Therefore, an important consideration in dual-use research is whether the research findings with dual-use possibilities should be disseminated and published. This makes it a difficult decision between academic freedom versus security. Moreover the German Research Foundation promotes an agreeable position that dual-use research should be regulated within the scientific system and institutionally with a view to protect science from political restriction, but they emphasise that it must be founded in professional, ethical actions, self-control and proper assessment by RECs. On the other hand, Salloch, took a more sceptical approach when she argues that RECs might not be appropriately suited for this kind of evaluation or able to prevent harmful activities (Salloch, 2018: 7).

In South Africa, where national environmental and biosafety measures are in their infancy, this challenging task to evaluate dual-use research will be one of the important responsibilities of the EBREC.

3.3.6 Indigenous knowledge and patent rights

Indigenous knowledge and patent rights in research is a thorny and sensitive ethical area. Trading with developing countries for rich natural resources is a concern because, on many occasions, the biological material from indigenous peoples is brought back to the lab by researchers and, in the end, patented as their own. Researchers commit biopiracy when they draw on the traditional knowledge of local people regarding plants, animals or chemical compounds or take biological resources without permission. It also applies to agricultural products. An EBREC should be aware of research actions that violate indigenous knowledge.

In 2015 French researchers were accused of ethical misconduct in the case of *Quassia amara.* The accusation was that they had stolen traditional knowledge of the indigenous people in French Guiana. The researcher interviewed the local people regarding the plant *Quassia amara's* antimalarial properties and published the preliminary research in 2005. After many years of research, they applied to patent a natural bioactive molecule against malaria and

cancer. The researchers did not find the compound from traditional preparations but used an alcohol-based extraction method. However, it was still considered the Guianese indigenous knowledge, and agreements should have been in place before the research began (Bourdy, 2017: 290–297).

The concept of "access and benefit sharing" or the claim of ownership of (indigenous) knowledge provoke ethical issues regarding social justice. As cited by Chennells, Ruth Macklin indicates that concerns regarding justice in research have "focused mostly on worries about the exploitation of human research participants or indeed of entire populations in the developing countries" (Chennells, 2014: 30). In South Africa, the most exploited indigenous group is the San people. Many examples of research with the San people were based on exploitation, being it DNA research or indigenous knowledge regarding plant technology and benefits, such as the well-known Rooibos-, Hoodia[34]- and Buchu plants (Chennells, 2009: 147–153). Many companies globally and in South Africa benefitted from the traditional knowledge of plant varieties and the medicinal value thereof without sharing the profit and acknowledgement with the San Community.

Roger Chennells, an attorney in Stellenbosch, who specialised in human rights law, assisted the San with traditional knowledge rights for many years. He assisted the San to become the first indigenous group to develop a research Code of Conduct and the traditional leaders developed the code. Except for the human exploitation and lack of respect and honesty in this vulnerable community, the lack of justice and fairness regarding the San's traditional knowledge were outlined as sensitive ethical issues (TRUST, 2017).

In 2003 the Council for Scientific and Industrial Research was forced into negotiations with the South African San Council and the National Khoisan Council for a benefit-sharing agreement. The agreement was negotiated related to the Hoodia succulent for its appetite- and thirst-suppressant properties. This agreement is celebrated as the first viable example of securing financial benefits for indigenous people (Chennells, 2009: 149). The second San benefit sharing agreement was signed in 2008 for the traditional knowledge of the sceletium plant, now used in Zembrin, a product for anxiety, stress and depression (Schroeder *et al.,* 2020: 286). The Rooibos Benefit Sharing Agreement was the third signed in 2019.

[34] The case of the succulent Hoodia plant is an example of cultural exploitation in South Africa. The Hoodia plant was used by the indigenous San people to control hunger and thirst. The South African Council for Scientific and Industrial Research (CSIR) patented the active ingredients of the plant without the knowledge or consent of the San community although it was based on the traditional knowledge of the San people. The CSIR was later forced to sign a benefit-sharing agreement with the San (Wynberg, 2016).

Besides indigenous people, farmers can also be exploited. Historically universities have been the leaders in innovative research to assist farmers with knowledge and technology transfer to improve crops and livestock. Patenting new research inventions provides a basis for licensing and selling for the researcher. However, commercial exploitation should be identified as a crucial ethical concern. The task of the EBREC in this regard should then be to ensure transparency and social responsibility on the side of researchers and to alert researchers regarding issues related to patent ethics. This, however, opens up another treacherous area for the EBREC to negotiate with researchers, since patent rights are not issued for a discovery but only for an invention. The Norwegian National Ethics Committee indicates that science is not patentable, but the technology, which is a solution to a problem, meaning the product, device, process or application may all be patented (The Norwegian National Research Ethics Committees, 2016).

In this regard EBRECs should also consider private industry, since it is one of the more significant research drivers sponsoring researchers to produce new products and patents for commercialisation. Unfortunately, big multinational firms invest privately in agricultural research, for example, keeping new inventions out of the public domain and often not directing the benefit of the research to resource-poor farmers of developing countries. The Norwegian National Research Ethics Committee confirms that matters related to research ethics need to address the benefit to the community in which the research is done, because a researcher has a responsibility to society at large. Issues of concern for an EBREC in this regard thus revolves around questions of global justice and the distribution of wealth. Also, how to advance knowledge and how to make the research accessible to be shared with society.

It is therefore perfectly legitimate for an EBREC to ask questions such as the following: Does the research constitute or contribute to biopiracy? Is there an unfair monopoly that will emerge from the research that excludes communities and individuals from a collective heritage? Are people excluded from the benefits obtained from the commercialisation of traditional knowledge? Does the monopoly badly influence the benefits or integrity of poor communities, jeopardising rural, small-scale farmers' sustainability or well-being? (Jogdand, 2015: 101). If so, the EBREC should make appropriate recommendations to researchers to prevent these questions from arising.

3.3.7 Ethics dumping

Ethics dumping was coined and defined by the European Commission (EC) in 2013 and entails the international unethical research practices from high-income countries on low and middle-income countries (LMICs) or communities. In the words of Prof Doris Schroeder from the University of Central Lancashire: “Exporting unethical practices to low- and middle-income

countries have become the new face of exploitative research" (Schroeder, 2012: 22). The researcher thus intentionally undertakes research in a LMIC that is prohibited in high-income countries with strict ethical rules. The uneven legal and ethical standards in LMICs open them up for exploitation in research. The objects of the exploitation could be human research participants, local communities, animals or the environment (Schroeder *et al.,* 2018: 2).

This kind of exploitation includes collaborations with a considerable imbalance in resources, knowledge and power. The practice of not including local communities in the research process is the lack of good participatory practice. RECs and researchers should be aware of cultural sensitivities and avoid the violation of customary practices.

An example of ethics dumping issues is described by Tangwa, Browne and Schroeder with the Ebola vaccine trials when the epidemic broke out in West Africa in 2013. The case study was about an Ebola virus vaccine that was tested for safety and immunogenicity and was sponsored by one of the biggest pharmaceutical companies. This was a multi-country and multi-site trial across five sub-Saharan African countries; however, it was tested not only on a small healthy group of individuals but also carelessly on citizens, risking the safety and health of citizens with an unproven vaccine. The exploitation entails that participants in LMICs assume that they will benefit personally due to low education levels. Tangwa *et al.* (2018) indicated that the case raises ethical issues because it circumvents regulatory procedures that will be inconceivable in higher-income countries and they further suggest that the exploitation is not only about inadequate informed consent or no benefit-sharing but rather an exploitation of an inadequate system and research regulatory and governance framework in these countries. The double standards will be inconceivable in any high-income country due to procedural rules on acceptable ethical conduct of this kind of research (Tangwa *et al.,* 2018: 49–57).

In the same way, a Zimbabwean researcher, Dr Isaiah Mharapara, believes that agricultural research in Africa is based on Western and foreign principles and systems. He concludes that research over many decades ignored the local conditions, plants, insects and organisms in Africa. He indicated that alien plants such as tobacco and genetically engineered crops damaged the ecological systems, ruined indigenous knowledge, and created soil loss and biodiversity (Van Niekerk *et al.,* 2017).

Tangwa *et al.* (2018) also explain that achieving equity in international research is a pressing concern and the overarching question is how to avoid exploitation in lower-income countries. The examples above indicate the seriousness of the problem. Constraints as explained by Tangwa *et al.* (2018) include insufficient resources, lack of independence, pressure from sponsors, unequal treatment of applicants in reviews, a lack of expertise on ethical review or

an insufficient ethical review. Therefore, researchers see the gap in countries where they can sidestep restrictive legal and ethical rules. If a researcher needs access to agricultural resources or biological materials, cultural artefacts or non-renewable sources such as minerals, the custodian or owner should give prior informed consent. As the previous section indicates, any material or indigenous knowledge transfer should be governed by full consent and a formal agreement.

Poverty and vulnerability increase the likelihood of exploitation in communities. Researchers can easily exploit the situation and conduct research without ethical clearance in developing countries or cases where regulations on environmental protection and biorisk-related issues are non-existent or inadequate. Although, when they want to publish and realise they need approval, they unethically try to obtain it retrospectively. Jemee Tegli describes an example where an anthropological study in "resource-constrained Liberia" attempted to seek ethics approval after the study was conducted. In an attempt to avoid the review process and to cover for this inconsistency, the researchers described it as "emergency research" (Tangwa *et al.,* 2018: 6–7).

Rath (from the University of Vienna) furthermore emphasises that genome editing experiments with the lack of proper governance can have significant global security implications. According to him (Tangwa *et al.,* 2019: 108): "… the absence of international standards of governance may result in safety- and security-sensitive experiments being transferred to countries with less stringent oversight, which will have serious implications for trust in international research." The trouble lies mainly in the inconsistencies and governance of international biosafety and biosecurity rules and frameworks. Accordingly, one of the tasks of an EBREC is to be aware of this problem, and to act as a gatekeeper to counteract the inconsistencies and the lack of rules and frameworks in certain countries, particularly the country in which it is located. The committee should be knowledgeable about international documents and treaties, such as the Convention on Biological Diversity.[35] This is an example of a leading document to ensure safety in the development, application, exchange and transfer of biotechnology research and related products.

Proper assessment and careful consideration of sensitive ethical issues in EBR is thus evident. The following section will investigate the role and challenges of EBRECs when dealing with ethically sensitive research, and will summarise and explain the mammoth task required from EBRECs and the exceptional insights that the committee reviewers will need to direct researchers and the research process in the right, ethical direction.

[35] The Convention on Biological Diversity will be discussed in Chapter 4.

3.4 The role and challenges of EBRECs

The overview in Chapter 2, and the previous sections in this chapter, outlined the remarkable research and technology advancements, the diversity of research areas and the challenging ethically sensitive issues that fall within the mandate of EBRECs. This section will discuss the role and challenges that EBRECs face in light of these technological advancements and research that is done in these various areas.

Nicholas Rigaud confirmed this in a report on biotechnology and ethics that he compiled for the Organization for Economic Co-operation and Development (OECD)[36] in which he pointed out that addressing each innovation's ethical, social, technical and safety issues proves to be an arduous task for RECs (Rigaud, 2008: 41). The report also argues that science on its own could not provide adequate answers to questions of moral values and absolute notions such as biodiversity or nature, and underlined that ethical values often conflict (2008: 7).

The challenge with an ethical and biosafety review is, as I have pointed out above, balancing the protection of scientific freedom and transparency against the security of society and the possible risks related to harm that may result from EBR, or the misuse that can be made of the research itself. It confronts EBRECs with the very real question of weighing the pros and cons of EBR and doing so based on principles appropriate and sensitive to advances in this field. (ASSAf, 2007: 24). However, if it is already an arduous task to find and articulate these principles, let alone prioritising them, an additional problem lies in the fact that there are no limits to the explorative minds of scientists; therefore, EBRECs will constantly be challenged to review new, unknown research topics and innovative, but potentially very controversial technologies. EBRECs are thus placed in a highly precarious position of dealing with the unknown and the unpredictable, raising further questions about the “mechanisms”, structures and procedures that EBRECs should have in place to deal with what could very well turn out to be a “mission impossible”.

The important point underlying these complex challenges is that registered review committees at HEIs have a regulatory mandate. This mandate means reviewing and approving procedures and practices regarding multiple research activities in EBR and overseeing the biosafety of biohazardous materials in a contained environment. The EBREC also has the mandate to take action and suspend research activities that present harm, pose unforeseen risks or where

[36] The OECD is an international organisation that works together with countries and organisations worldwide to build better policies for better lives. They strive to establish international standards and to find solutions to social, economic and environmental challenges. South- Africa is a member country.

there are cases of non-compliance with regulations or the permissions granted as a result of the review process.

Part of the problem that I have set out to address in this thesis is that EBRECs in South Africa need to register with the NIH, the USA National Institute of Health, due to a lack of a national registration body for EBR in South Africa The national body in South Africa, the NHREC, registers Human Research Ethics Committees and Animal Research Ethics Committees but is not yet geared to register EBRECs. In this regard, part of the mission of the NIH is to promote the safe conduct of research involving recombinant or synthetic nucleic acid molecules. Although the mandate of the NIH to regulate institutional EBRECs is quite extensive, institutions are mostly self-regulating (Rainer & Cook, 2016: 74). Since there is an increase in the types and complexity of research projects in disciplines such as physical sciences, engineering and chemical engineering, aerospace, material sciences and others, movement in research is beyond the traditional boundaries (ibid, 2016: 76). Rainer and Cook recognise that the NIH guidelines are an essential regulatory tool and safety framework, but they point out that numerous projects that will appear on the radar screen of EBRECs will not always be explicitly covered from an operational perspective by the guidelines prescribed by the NIH (2016: 77). Rainer and Cook further indicate that while the NIH guidelines provide an essential health and safety framework for committees, numerous projects are not covered (Rainer & Cook, 2016: 76). They mentioned some examples that are not explicitly defined within the scope of the NIH guidelines, such as “Dual Use Research of Concern”, “Gain-of-function research” and “Engineered Nanomaterials” (2016: 76). Therefore, this situation puts additional liability on EBRECs to protect the researcher, institution, community and environment effectively. As such the NIH regulates certain areas within applicable guidelines. These are highlighted below:

- recombinant or synthetic nucleic acid molecules, including their use in animals (including arthropods) and plants;
- biological materials that may contain micro-organisms or viruses infectious to humans, animals or plants (e.g., parasites, viruses, bacteria, fungi, prions, rickettsia);
- toxins (human, animal or plant);
- substances such as blood, body fluids, cell lines or tissues, derived from humans and other primates; and
- biologically active agents, causing disease in humans or that will have a significant impact if released into the environment (e.g., toxins, venoms) (Rainer & Cook, 2016: 74).

In line with the above, in HEIs ethical and biosafety approval is mandatory prior to the start of any research project. To obtain and use any of the abovementioned biological materials or processes, it is the task of an EBREC to review, approve or reject the project. In my experience, researchers in environmental and biosafety sciences see ethics as a hurdle they need to overcome, with the attitude, “I must get ethics, to run my experiment”. They do not see it as a tool to enhance ethical and research practices. This attitude could be due to inadequate principles and guidelines or an insufficient ethics strategy. It could also be that those commonly accepted principles are restrictively applied or improperly used (Australian Law Reform Commission, 2010: 6.66).

Furthermore, some areas of EBR are not necessarily well regulated but cannot be excluded from a proper review before the commencement of research. Non-regulated environmental research is evident in the following example. Suppose concentrated fertiliser is introduced into a lake or river to evaluate the effect on the fish population. In that case, ethical approval is required from the animal research ethics committee because the test subject is an animal species. However, if the same fertiliser is introduced to test algae's effect in the lake or river, ethical approval would not necessarily be required; however, it will have precisely the same impact on the fish and the environment or ecology in both cases. This problem also emphasises the lack of collaboration with the other Ethics committees, such as the Animal Ethics Committee.

With this complexity in mind, it is evident that interdisciplinary teams are crucial to support ethical reviews and act simultaneously as safety gatekeepers for the many different and sometimes complicated and risky research protocols. The committee should engage in an intensive review of the protocol to ensure that the appropriate biosafety containment level and reasonable safety precautions will be considered to mitigate any risks. This high-level review without a framework, applicable guidance or a set of principles to assist in the review process is a daunting and sometimes impossible task. Moreover, it can put the committee in a dangerous and vulnerable situation because they can be held responsible for serious adverse events.

To illustrate this interdisciplinary dilemma, Rainer and Cook propose a case study as an example (2016: 77). Suppose a team of researchers form a group that will look at a specific plant. They want to study the whole plant and improve relevant traits such as: 1) improving shelf life, 2) limiting potential damage during shipment and 3) maximising food safety. The study requires a world class facility, interdisciplinary teams and business and academic partnerships. The study consists of a diverse group of researchers.

> The first group investigates the mathematical modelling and engineering to understand the underlying networks that contribute to traits and yield variability wanted by consumers.
>
> The second group will look at plant disease, plant-fungal interaction, plant biotic stress, transgenic plants for disease resistance, virus disease, the ecology of plant biotic interactions and sustainable agriculture for developing countries.
>
> The third group will be an abiotic stress group, studying extremophile genes for engineering plant stress tolerance, drought stress, system biology, physiological ecology of plants, drought ecology, climate change and the plant response to osmotic stresses.
>
> The fourth group will investigate nutrient stress, evaluate systems biology, plant iron and nutrient stress and model regulatory pathways, characterising soil micro-organisms and microbial processes using culture-dependent and independent methods (2016: 77).

The task of an EBREC is clearly to review, assess and approve this multidisciplinary and complicated project. The committee's task is also to ensure that the research proposal meets all the ethical requirements and national legislation. Therefore, evaluation should be based on ethical principles related to the specific kind of research. The review process will involve reviewers with expertise in the mentioned fields, an ethicist, a biosafety officer and a community representative. Equally important is an expert in Risk Management and an expert in applicable laws with knowledge of permits and codes of conduct in the different fields. Thus, it is evident that members need to be from many different backgrounds and fields of expertise to provide a proper multidisciplinary and justifiable assessment.

The case study and discussion illustrate some of the complexity of EBR projects, which, if not clearly acknowledged and well-managed, may lead to inconsistent reviews and outcomes. An article in the Bratislava Medical Journal that confirms the above, mentioned that the IRBs use different frameworks and that the reviewers lack a tool for the decision-making process. It, unfortunately, led to inconsistent decisions regarding the same study (Ekmekci & Guner, 2019: 96).

To prove this statement, Green *et al.* (2006) show in a survey that for the same study, 43 IRBs decided in favour of an expedited review, 31 requested a full board review, and one IRB rejected the study due to the risks involved. The survey thus confirms the problem of inconsistencies. Different reasons for the inconsistent outcomes or decisions were mentioned in the article. Subjective factors such as beliefs, personal attitudes, feelings and irrational

influences from committee members can significantly impact human and animal research outcomes. With EBR, inconsistent review outcomes are usually due to the lack of expertise, knowledge and suitable ethical frameworks with applicable guidelines and principles. Ekmekci and Guner (2019) conclude that it is impossible to avoid variation in the decision-making process altogether. Still, they agree that subjective decisions based on irrational criteria can be minimised if the decision-making criteria are "according to internationally accepted guidelines to cover the basic ethical criterion" (Ekmekci & Guner, 2019: 100).

Further to this, the Academy of Science in SA (ASSAf), undertook a study in 2015 to determine how well research facilities in South Africa deal with ethical issues in EBR, laboratory biosafety and biosecurity measures (ASSAf, 2015: 60). The mentioned study gathered info through a national survey that revealed a lack of adequate knowledge regarding national and international conventions, laws, policies and research activities. The study findings indicate that the research community in EBR is not informed enough regarding mandatory ethical and legal practices (ibid: 2015: 83). The ASSAf study suggests the following: "South Africa should establish clear, encompassing and balanced ethical guidelines for all life science research and development work to ensure our safety and the integrity of the environment we live in" (2015: 28). The current challenges for EBRECs are apparent, the lack of guidance is concerning while the responsibilities are quite extensive. The obligation of EBRECs continue to expand as new technologies evolved, but they are not necessarily prepared or equipped for the task. Compared to Animal or Human Ethics committees, EBRECs have a more significant regulatory burden and handles a much broader science range but without a well-established national regulatory system.

Ekmekci and Guner emphasised that international documents with principles and guidelines need to be well covered and reviewers well trained and knowledgeable (Ekmekci & Guner, 2019: 96). Therefore, it means that an ethics review committee or review board needs a "toolkit to regulate the ethical decision-making process" (ibid: 2019: 96).

3.5 Conclusion

Environmental and biosafety concerns are eminently diverse, from spreading transgenes into the environment to the negative impact on different species, creating superficial organisms and tampering with nature, as indicated by the examples discussed above. In modern biotechnology, with its "rainbow of colours" and applications, researchers strive to find the pot of gold at the end of the rainbow.

This chapter and the previous one discussed the supporting questions to furnish the background information to understand environmental research ethics and biosafety research

ethics. I have used a number of practical examples in order to do so, I have elaborated on important terminology in EBR and I have explained how environmental and biosafety research ethics are related and intertwined.

EBR and its applications strive to solve global environmental, food and medicine issues or enhance humans' living conditions. However, it does not matter how beneficial it seems, there will always be drawbacks to this research. Modifications to living organisms are a risk due to unforeseen consequences and therefore need solid ethical consideration. The ability to create a pre-selected change in germ and somatic tissues of living organisms through genetic engineering equally raises unresolved legal, social and ethical questions, while perceptions of risk in biotechnology are embedded in cultural, social, religious and political values (Harrell, 2017: 2).

The chapter also elaborated on the many challenges that EBRECs face, dealing with the intense complexity that it must deal with in this vast interdisciplinary field without proper governance and guiding frameworks. New knowledge gained from research is crucial but can, unfortunately, be used in a good or bad way for life on Earth. The misuse of research applications can cause global damage. Therefore, ethical limits need to be set by EBRECs and sensitive ethical areas addressed. Socially acceptable research will contribute to supporting all stakeholders and will make EBR more truthful.

With the scene set and my supporting questions answered, Chapter 4 will deal with my first main normative research question. I will explore and elaborate on the current state of ethical principles in EBR. I will also dig into assessment frameworks, national and international regulation, legislation and declarations.

CHAPTER 4: THE CURRENT STATE AND APPLICATION OF PRINCIPLES IN THE RESEARCH AREA OF EBRECs

4.1 Introduction

Chapters 2 and 3 highlighted the complexity, dynamics and uncertainties of the trans- and inter-disciplinary research field of, and the need for proper ethical assessment in EBR. Applying fundamental and uniform ethical principles provides the firm foundation that leads the researcher in the right direction in the research process. In my first chapter, I have indicated that this study aims to fill significant lacunae in the research literature concerning applicable and overarching principles for EBRECs. This chapter will mainly discuss Universal Codes, Rules and Principles foundational to the decision-making process in RECs. I will also elaborate more specifically on globally existing principles and guidelines in the environmental and biosafety research ethics arena. I will thus answer my first main normative research question in this chapter: *What is the current state of ethical principles for ethics reviews in the field of environmental and biosafety research ethics? Which principles are currently used in this context, and how?*

However, it is necessary to first determine if principles for ethics review are the preferable option to follow, as principlism in research ethics reviews is challenged in some literature, promoting casuistry instead. This chapter's introductory part will thus investigate and evaluate the casuistry approach in contrast with principlism.

With all related scenarios in mind, the chapter will conclude with a proposal of a broad ethical framework for the reviews done in EBRECs. The illustration below is a useful starting point to explain the interrelated aspects of considerations that need to taken up in a framework for ethics reviews and assessments.

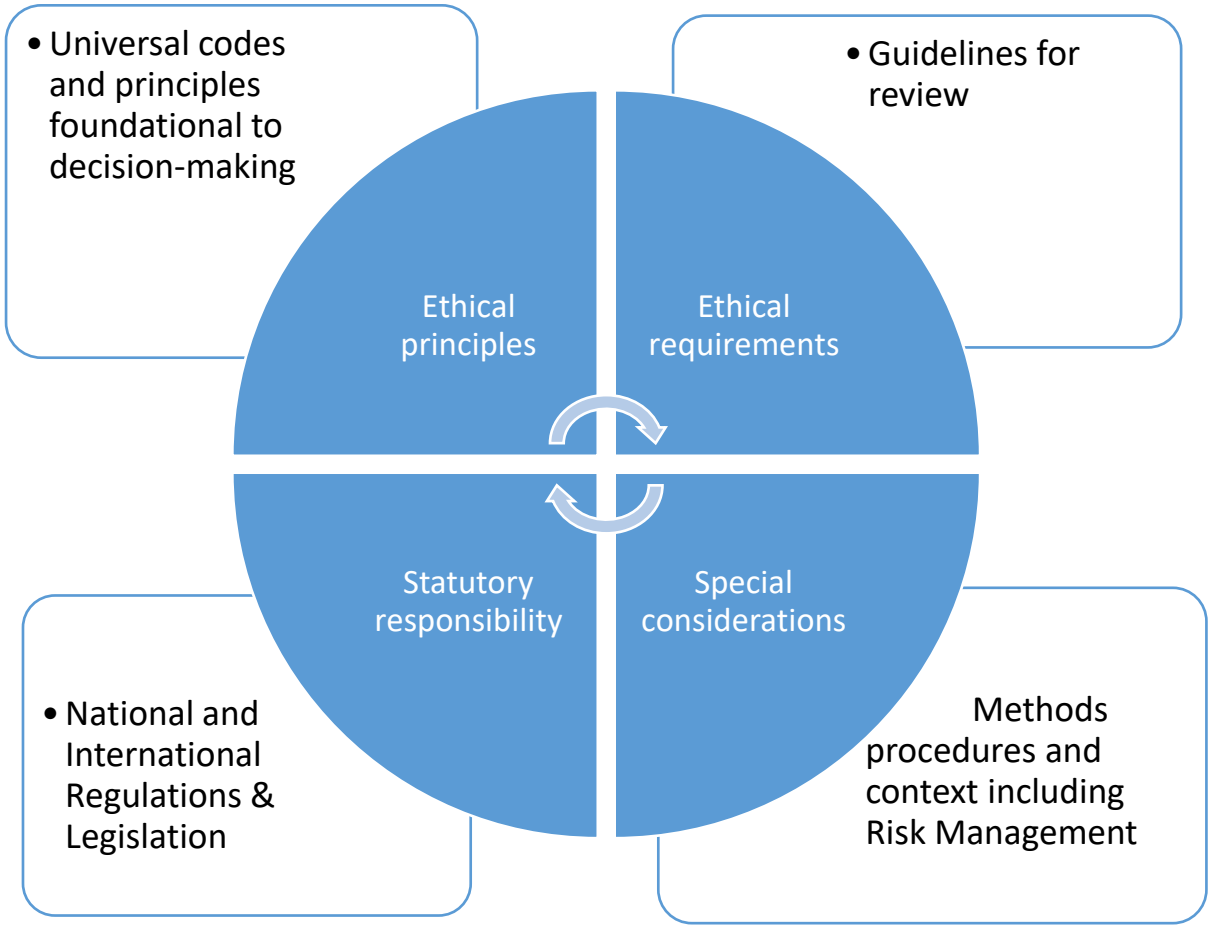

Figure 4: *Ethical Framework* (Adapted from Hoffman & Visagie, 2017: 5)

4.2 Ethical assessment approaches: Principles vs Casuistry

Ethical principlism was introduced in the 1970s in medical ethics as a method to analyse ethical issues. Principles draw on values shared by many people, irrespective of their philosophical preference, being that of a Kantian Deontology, a Utilitarian Consequentialism or any other ethical theory. The concept of a principlist approach in moral decision-making is based on the idea of a universal morality that is objective and shared by all rational humans (Davis, 1995: 55). Such shared ethical principles then assist the ethics committee reviewers in reaching an agreement on ethical issues that are significant in everyday real-life situations and decisions.

Robert Nozick from Harvard University explains the need for principles and why we need to adhere to them when he indicates that principles place action under “general rubrics”. Actions that are linked can be viewed or treated similarly (Nozick, 1991: 117). He further indicates that justification by general principles works in two ways, using the principle to reach a correct

decision and using the principle to constrain the influence of personal preference and irrelevant factors and therefore guide us to the right decision or judgement (1991: 124).

According to this view, for research to be transparent and honest, it should follow principles that are universal and objective, and, according to Beauchamp and Childress, are beyond culture, individual vagaries and traditions and need to be drawn from a "common morality". (Beauchamp & Childress, 1979: 3). This implies that moral deliberation aims to achieve a goal of unity and consistency that can be explained or justified by rational argumentation. To accomplish this goal, Beauchamp and Childress advocate principlism to guide ethical decisions. This approach to ethical decision-making has been widely adopted on many levels and ethics fields, primarily because it sidesteps long debates in moral philosophy. Rather than engaging in a philosophical discussion of the most suitable method or theory at a normative level (for example, virtue ethics, deontology or teleology), principlism provides a practical way of addressing real-world ethical dilemmas. While this approach can be linked to and even grounded in normative ethical theories, it is not associated with any single theory. Beauchamp and Childress rather argue that principles are widely understood and accepted within society, while that is not necessarily the case with ethical theories (Chatfield, 2018: 31).

Principlism, or relying on principles in the ethical decision-making process, prescribes a systematic, consistent and unified approach. Therefore, Beauchamp and Childress claim that it provides a secure method and the necessary vocabulary to identify and articulate ethical concerns and arguments. It also offers an ethical framework to analyse and address many complex issues in the human and bioethics sciences. This framework also fits other areas such as allocating scarce resources, new reproductive technologies and genetic engineering as well as many more research fields. They also claim that it caters for people from different cultural backgrounds and world views (Beauchamp & Childress, 1979: 3).

In contrast, casuistry is mentioned as an alternate form of ethical decision-making. Jonsen, as cited in (Loue, 2007: 46), calls it a case-based system of ethical analysis. Whereas principlism is based on a set of principles to be applied in a specific case, Jonsen indicates that casuistry alternatively represents a particularised, context-driven and case-based normative decision-making method (Tremblay, 1999: 492). It means discovering ethical principles in the cases to be analysed themselves and that the applicable principles are linked to their actual surroundings (Jonsen, 1995: 245), they do not “fly in”, as it were, from a general, abstract source of principles “located” somewhere else. Loue called principlism the "top-down" approach to resolve ethical dilemmas by applying a given set of principles. On the other hand,

casuistry is the "bottom-up" or case-based[37] approach, where the principles are derived from analysing the situation at hand (Loue, 2007: 46). Loue explains it as follows: "The ultimate view of the case and its appropriate resolution comes, not from a single principle, nor from a dominant theory, but from the converging impression made by all of the relevant facts and arguments that appear ..." (Jonsen, 1995 as cited in Loue, 2007: 46).

Debra Erickson from Bucknell University argues that casuistry or case-based reasoning should be used in environmental ethics (Erickson, 2016: 287). She points out that the practice of casuistry developed over the years in response to real life moral dilemmas, taking the context and surroundings seriously in the decision-making process. In fact, Erickson argues that casuistry developed precisely in response to the moral crises that are perceived when it is realised that principles alone do not provide the answer, and does not help to arrive at the morally correct decision (2016: 287).

Paul Cudney (2014: 208) compared the two approaches and indicates that principlism and casuistry are not radically divergent. He argues that both recognise the need for moral principles. Conversely, Beauchamp and Childress argue that with principlism, the morally relevant considerations need to be balanced and that the basic principles establish only a prima facie obligation. The reason being, according to the specific case in question, some principles could be outweighed by another more important principle (2014: 212).

Similarly, Cudney argues that while the principlist and the casuist language may differ, their methodological views are very similar (2014: 215). With both approaches, the need to apply prima facie principles in a given case is necessary. But with casuistry, rhetorical reasoning is used with the interpretation of cases while the principlist approach focuses only on the moral principles. Jonsen and Toulmin articulated it as "applying maxims[38] to a case" and relying on "paradigm cases"[39] when needed or in the case when multiple maxims apply (2014: 215). The similarity between the two approaches lies in the fact that both methods will look at past judgments to reach an agreement on how to apply principles or maxims. However, Cudney

[37] Jonsen defined “case” as follows: “A case is a confluence of persons and actions in a time and a place, all of which can be given names and dates. A case, we say, is concrete as distinguished from abstract because it represents the congealing, the coalescence, or the growing together (in Latin, *concrescere*) of many circumstances. Each case is unique in its circumstances, yet each case is similar in type to other cases and can, therefore, be compared and contrasted. Cases can be posed at various levels of concreteness. Some will be composed of quite specific persons, times, and places; others will describe an event or practice in more diffuse terms” (Jonsen, 1995: 241).

[38] “Maxim” is defined by Merriam-Webster and the Cambridge English Dictionary as a “general truth, fundamental principle or rule of conduct”

[39] Paradigm cases according to analytic philosophy is an accusation that certain concepts or terms are meaningless but that the regular application of certain terms put some kind of definition in place. In other words a case that falls under its common definition of term. Or according to the Oxford Dictionary: “A case or instance to be regarded as representative or typical” “Paradigmatic cases are carefully selected examples from phenomena” (Mills, 2010).

acknowledges that principles and maxims are not always equivalent to each other, but he also stated that the difference does not result in significant methodological differences.

Conversely, John Arras sees casuistry as a commitment to a type of “immaculate perception”: cases are portrayed to speak for themselves. He appeals to the limits of casuistical ethical decision-making, arguing that the casuist case analysis cannot supply us with relevant principles that can be generalised from case to case (2014: 255). On the contrary, Cudney feels that both principlism and casuistry can be beneficial in the decision-making process. He sees principlism and casuistry as the same method, just used in a different way. Both methods include the use of principles but they are applied differently. The former focuses on the moral principle to solve the case and the latter examines the case before applying a principle.

Given the multidisciplinary nature of EBR, I agree with Cudney's point of view and suggest that Principlism needs to be the primary method for the decision-making process of an EBREC, while taking into account the context and surroundings in which the research will be conducted. The latter is indeed particularly important in complex cases. As Cudney concludes: if we take "principlism with its reliance on common morality and casuistry with its reliance on judgments about cases, each represents an attempt to ground moral judgment in facts that are independent of the beliefs or norms of any particular person or society" (2014: 228). Therefore, I am of the view that casuistry combined with principlism could be helpful for ethical decision-making in the complex EBR arena. Casuistry could be a critical evaluation method or a technique to justify specific actions (Tomlinson, 2012: 112). However, I argue that principlism always needs to be the primary method in the decision-making process of EBRECs, while casuistry may be a useful additional tool in cases of uncertainty.

With the argument regarding the use of principles or casuistry discussed, I will now dig into the statutory responsibilities, different international principles, frameworks and universal codes to find the best available answer on my main research questions.

4.3 International frameworks and universal codes

The literature emphasised the importance of accepted guidelines and principles throughout the previous sections to guide the ethics assessment process. The literature on the topic admits that EBR faces a diversity of challenges due to the broad field this research entails. While humans and the protection of humans always need to be considered in any area of study, a much more comprehensive view is necessary when dealing with EBR. There is a human factor in any research project that needs consideration during an ethical assessment being it the researcher themself, the subjects, an owner of the specific research environment, a farmer, the community or society or the sponsor. It is thus evident that principles in the EBR

context need to cover all scenarios and not err by effectively excluding the consideration of humans.

In order to answer the first normative research question of the study regarding the state of ethical principles in EBR and the use of principles in the research ethics process, it will be necessary to take a step back and to take a glance into history and the development of national and international ethical frameworks, codes and legislation. Multi-national and multidisciplinary documents acknowledged and used by Research Ethics Committees (RECs) globally originated in bioethics. In 1966, Health Services in the USA issued the first set of regulations and requested the establishment of RECs or review boards. This was revised in 1971 and 1974 and created a turning point in the history of research ethics codes (Greenwald, Ryan & Mulvihill. 1982: 207).

The first ethics codes, the Nuremberg Code (first edition 1947), outlined the foundation of ethical conduct. The Declaration of Helsinki (first edition 1964) set the stage for contemporary human subjects ethics committees and the principle of informed consent. These two documents initially only focused on researchers and the welfare of research subjects and not specifically on committee reviews (Levine, 2004: 2312).

4.3.1 The Nuremberg Code (1947)

The Nuremberg Code, introduced in August 1947 after the horrific experience of human experimentation during WWII by the Nazi doctors, aimed to protect human subjects. It attempted to give clear rules about what is and is not ethical when conducting human experiments. The Nuremberg Code does not carry the force of law but was the first international document that advocates voluntary participation and informed consent as primary guiding principles of research. The code consists of ten points focusing on human rights of research subjects and will be applicable in EBR where people are involved. To put it even more strongly, there indeed is a human factor in any EBR research project that needs consideration during an ethical assessment, be it the researcher themself or any person involved such as an owner of the specific research environment, a farmer, the community or society or the sponsor. Accordingly, the Nuremberg Codes continues to be a relevant point of reference for EBR research. In fact it gives an excellent overall code of conduct for research activities in any research field[40] (2004: 2312).

[40] See Appendix B for more detail about the Nuremberg Code and other guidelines and framework documents discussed in this chapter.

4.3.2 The Declaration of Helsinki (1964)

The World Medical Association has developed the Declaration of Helsinki as a statement of ethical principles to guide physicians and other participants in medical research involving human subjects. Medical research involving human subjects includes research on identifiable human material or identifiable data (WHO Bulletin, 2001: 373). This declaration forms the basis for Good Clinical Practices for research combined with clinical care and non-therapeutic research, but is also not a legally binding document. The declaration's applicability in EBR is related to the declaration's leading position to protect humans from potentially harmful research projects. Building on the Nuremberg Code, this declaration consists of 32 human- and medical-related principles, the most prominent of which are 1) in medical research on human subjects, considerations related to the well-being of the human subject should take precedence over the interests of science and society and 2) medical research is subject to ethical standards that promote respect for all human beings and protect their health and rights. Some research populations are vulnerable and need special protection and 3) Research investigators should be aware of the ethical, legal and regulatory requirements for research on human subjects in their own countries as well as applicable international requirements. No national ethical, legal or regulatory requirement should be allowed to reduce or eliminate any of the protections for human subjects set forth in this declaration.

4.3.3 The Belmont Report (1979)

In response to the scandal around the Tuskegee Study of Untreated Syphilis in the Negro Male that was conducted between 1932 and 1972, the Belmont Commission was formed in the USA to determine what went wrong and to make recommendations on measures and guiding principles that can prevent such horrors from being repeated in future. In their own words, they summarised their mission as follows:

> The [American] National Commission wrote the Belmont Report for the Protection of Human Subjects of Biomedical and Behavioral Research. The Commission, created as a result of the USA National Research Act of 1974, was instructed to identify the basic ethical principles that should underlie biomedical and behavioural research involving human subjects and develop guidelines to ensure that such research is conducted following those principles. Informed by monthly discussions that spanned nearly four years and an intensive four days of deliberation in 1976, the Commission published the Belmont Report [in 1979], which identifies basic ethical principles and guidelines that address ethical issues arising from the conduct of research with human subjects (The Belmont Report: HHS).

The three broad ethical principles articulated in the Belmont Report remain the most prominent guiding framework in research on human participants today, relevant, and universally applicable research ethics principles in any research area, and accordingly, will also be

relevant to EBR where humans are involved. The most prominent principles articulated in the Belmont Report are respect for persons, beneficence and non-maleficence and justice – principles that are also taken up in the principlist guidelines of Beauchap and Childress.

4.3.4 Beauchamp and Childress – Principles of Biomedical Ethics – PBE Model (1979)

The PBE model outlined and defended the principlist ethical framework and is a well known and comprehensive guide in the ethical decision-making process of review boards. It incorporates the fundamental principles that need to be considered, but also explores the unique nature of a specific moral situation. The PBE-model promotes four basic principles that Beauchamp and Childress consider to be drawn from "common morality" and as such it has acquired canonical status and is internationally accepted. These four “core” principles can also be regarded as bioethical principles. As indicated in Chapter 2, the broad definitions of bioethical include moral issues in life sciences, biology, medicine, environmental, population and social sciences (Sateesh, 2013). These four principles are:

- autonomy: respect the views, choices, and actions of others
- non-maleficence: avoid causing harm
- beneficence: act for the benefit of others
- justice: treat people fairly (but also other living organisms and the environment)

(McCarthy, 2003: 66; Beauchamp & Childress, 1979)

4.3.5 CIOMS International Ethical Guidelines for Biomedical Research Involving Human Subjects (1991)

The Council for International Organizations (CIOMS) is part of the World Health Organization (WHO) and an international non-governmental organisation. It is under the auspices of the United Nations Educational, Scientific and Cultural Organization (UNESCO). The CIOMS guidelines reflect the advances of biomedical research in the 1980s and the controversies it raised[41] as well as changes in biomedical research ethics in response to that. Working in close collaboration with the WHO and UNESCO, the Council’s goal was to assist countries in defining national policies on biomedical research ethics. The principles in the guidelines are regarded as universal (CIOMS, 2016: xii). Formulated in its own words, the aim is as follows:

[41] Two controversial cases were the Baltimore and Gallo Cases. The Baltimore case was about an allegedly fraudulent paper. A postdoctoral fellow named Margot O’Toole worked in the laboratory of a cellular immunologist and she found serious faults with a paper from David Baltimore and his co-researchers and therefore acted as a whistleblower. The Gallo Case was the issue regarding the discovery of HIV in 1984. There was a dispute concerning who discovered the virus and how it was developed in a form useable for blood tests. The dispute was between Robert Gallo from the NIH and scientist of the Pasteur Institute in Paris. Gallo was accused of misappropriation and contamination.

> The Council for International Organizations of Medical Sciences (CIOMS) published International Ethical Guidelines for Biomedical Research Involving Human Subjects. The Guidelines relate mainly to ethical justification and scientific validity of research; ethical review; informed consent; vulnerability of individuals, groups, communities and populations; women as research subjects; equity regarding burdens and benefits; choice of control in clinical trials; confidentiality; compensation for injury; strengthening of national or local capacity for ethical review; and obligations of sponsors to provide health-care services (CIOMS, 2002).

What is of particular importance for EBRECs in these guidelines is the emphasis placed on informed consent by groups, communities and populations in the review process, as well as equity regarding the burdens and benefits of research.

4.3.6 A Universal Ethical Code for Scientists (2007)

Sir David King, the UK Government Chief Scientific Adviser, developed the “Universal Ethical Code for Scientists” in 2007. The code aims to raise awareness of ethical research issues among scientists and secure public support for science.

Based on societal values, the code of conduct includes three principles, but it supports the development of more "detailed discipline-specific principles". The three principles that are also relevant to EBR are Rigour, Respect and Responsibility:

- Rigour: Rigour, honesty and integrity
- Respect: Respect for life, the law and the public good
- Responsibility: Responsible communication: listening and informing
  (King, 2007)

Sir David acknowledged the challenges of science and demands from the public sector for ethical practices and to "serve the wider good" (King, 2007). Thus, this code is a general statement emphasising the values and responsibilities of researchers in conducting research in any form or shape, EBR included.

4.3.7 The Singapore Statement (2010)

The Singapore Statement on Research Integrity was developed to promote ethical conduct among scientists around the world. It provides a framework to promote global research integrity. It was established during the Second World Conference on Research Integrity, 21–24 July 2010, in Singapore, to act as an international guide to the responsible conduct of research. The statement intends to provide ethical guidance to governments, scientists and organisations to develop comprehensive codes, standards and policies to promote research integrity globally. The attendees covered more than 51 countries, and since 2010 has gained wide acceptance within the research and review board community (Resnik, 2009).

The Preamble of the statement states the following:

> The value and benefits of research are vitally dependent on the integrity of research. While there can be and are national and disciplinary differences in the way research is organised and conducted, there are also principles and professional responsibilities that are fundamental to the integrity of research wherever it is undertaken (Singapore Statement, 2010).

The Singapore Statement on Research Integrity consists of four Principles and 14 Responsibilities. The four Principles are:

- honesty in all aspects of research;
- accountability in the conduct of research;
- professional courtesy and fairness in working with others; and
- good stewardship of research on behalf of others.

The fourteen responsibilities "address such topics as data integrity, data sharing, record keeping, authorship, publication, peer review, conflict of interest, reporting misconduct and irresponsible research, communicating with the public, complying with regulations, education, and social responsibilities" (World Conference on Research Integrity, 2010). As such, the Singapore Statement principles apply to research in any discipline as a general framework for research integrity, EBR included.

The challenge to promote global scientific integrity, however, is acknowledging the cultural, economic, political and social differences among countries. This influences the conduct of research and the applicable ethical norms (Resnik, 2009). The Singapore Statement, however, acknowledges these differences, but also embraces the common standards for research ethics, which transcend national boundaries. It should also be borne in mind that The Singapore Declaration is not a regulatory document but rather a global guidance document.

With the leading international frameworks and universal codes in research ethics mentioned and explained[42], the next section will focus on other regulatory documents and protocols applicable to the EBR environment.

4.4 Statutory responsibility: National and international regulations, legislation, protocols and studies

Modern biotechnology creates new exciting opportunities but, at the same time, poses potential risks globally. The general expectation of society is that researchers should take responsibility for their actions and abide by regulations, legislations, protocols and codes of

[42] Appendix B provides the links to the embedded original documents for all the above International Frameworks and Codes.

conduct. Accordingly, international and national frameworks and protocols need to be considered in the research process. Countries worldwide, however, differ considerably in developing, applying and regulating biotechnological advances, creating tension in international economic and socio-political relations, which are all further complicating factors that EBRECs will need to consider in their reviews.

Against this background it must be emphatically stated that there is no comprehensive international legal instrument for biotechnology or biotechnology products, but there are international agreements, or the so-called “soft laws”. Several international organisations[43] have set standards regarding biotechnology's impact on the environment, agriculture, food security, scientific innovation, socioeconomics, trade, health, human rights and ethical aspects (Horng, n.d.: 2). These international bodies made substantial efforts to highlight biosafety, biosecurity and environmental demands and challenges, leading to agreements and requirements that aim to regulate and guide research activities and promote safety on many different levels.

Knowing and understanding all the agreements and requirements can be an overwhelming and challenging task for the researcher and the EBREC, who needs to evaluate compliance. An investigation into the different statutory responsibilities does not fall within the scope of this study; however, it can be worthwhile to consider it for future research studies. Nevertheless, for the purposes of my study it is necessary to mention some significant statutory responsibilities as it will assist in understanding the challenging task of EBRECs and determine how it could influence applicable ethical principles.

It is not easy to make sense of the extensive list of regulatory documents relevant to the application and impact of research and biotechnology. Regulatory systems broadly cover international protection of 1) the environment, 2) international trade law, and 3) human rights. (Herdegen, 2010), but in many cases they can also be more specific, for instance, some instruments that regulate agricultural biotechnology address three main aspects: biosafety and environmental food safety, access to genetic resources and sharing of benefits and intellectual property rights. Below only a few of the more well-known and applicable regulatory instruments are mentioned for the purpose of this study.

[43] Organisations include: Codex Alimentarius; World Health Organization (WHO); United Nations Food and Agriculture Organization (FAO); United Nations Environmental Programme (UNEP); United Nations Educational Scientific and Cultural Organization (UNESCO); the United Nations Industrial Development Organization (UNIDO), and the World Trade Organisation (WTO).

4.4.1 Universal Instruments (Soft law)

4.4.1.1 Environmental Protection

- **U.N. Convention on Biological Diversity (CBD)**

The Convention on Biological Diversity (CBD) was negotiated under the authority of the United Nations Environmental Programme (UNEP) in the early 1990s. Regarding environmental research, the CBD is probably the most prominent international convention for the protection of the environment and an international legal instrument. It addresses conservation, sustainable development, prevention of species extinction, handling of genetic materials of plants, animals and micro-organisms and other topics that are in the interest of "safeguarding life on earth" (Weinbaum, 2019: 44). The Convention declares that "benefits to humans should not be at the expense of biodiversity and sustainability of the ecosystem" (2019: 44). Two supplementary and well-known agreements of the CBD are the Cartagena Protocol and the Nagoya Protocol.

- **Cartagena Protocol on Biosafety**

The *Cartagena Protocol on Biosafety*, an international protocol, was adopted in 2000 and came into force in 2003. This CBD associated protocol addresses risks for humans and the ecosystem when handling live organisms in modern biotechnology. The modifying of plants and animals genetically and biochemically to create LMOs, as indicated in Chapter 2, requires proper safety assessment. Accordingly, the implementation of protocols and procedures on a national and sub-national level became essential.[44] The main objective of the Cartagena Protocol is:

> [t]o contribute to ensuring an adequate level of protection in the field of safe transfer, handling and use of living modified organisms (LMOs) resulting from modern biotechnology that may have adverse effects on the conservation and sustainable use of biological diversity, taking also into account risk to human health and specifically focusing on transboundary movements (CBD Article 1: 3).

The Cartagena Protocol builds on Principle 15 of the Rio Declaration and the precautionary approach (Jungcurt & Schabus, 2010: 197) and is acknowledged as a powerful international instrument in the biosafety area.

[44] As a general rule, international agreements or universal instruments on biosafety should be translated into national regulations and laws and coordinated frameworks.

- **Nagoya Protocol on Access and Benefit Sharing**

The 2014 *Nagoya Protocol on Access and Benefit Sharing* provides a legal framework and international agreement for data collection permission abroad to research genetic resources and traditional knowledge. The aim is benefit sharing in the utilisation of genetic resources to ensure that it is done in more a equitable and fair way. Article 14 of the Protocol makes provision for a platform to exchange information on benefit-sharing and access with the Access and Benefit-sharing Clearing-House (ABSCH). This is a key tool to facilitate the implementation of the protocol, hosting relevant information and provide genetic resources of traditional knowledge and opportunities to connect users and to assist researchers (Convention on Biological Diversity, 2021).

Additional Universal Instruments for Environmental Protection[45]

Other universal instruments in the international arena aiming at environmental protection include:

- The International Plant Protection Convention (IPPC) which came into force on 3 April 1952
- The International Convention for the Protection of New Varieties of Plants (UPOV) of 1961 was revised in 1972, 1978 and 1991.
- The International Treaty on Plant Genetic Resources for Food and Agriculture is an international agreement of the United Nations with the framework of the Food and Agriculture Organisation which came into force on 29 June 2004.

4.4.1.2 International Trade protection

Worth mentioning in this context is also a number of agreements with the primary aim of protecting international trade, which also has implications for EBRECs and the research conducted in its ambit.

Agreement on the Application of Sanitary and Phytosanitary Measures (SPS)

The SPS is a World Trade Organization (WTO) agreement that entered into force in January 1995. It regulates the application of food safety and animal and plant regulations. It is an international trade law to promote global harmonisation and it sets out animal and plant health standards and the basic rules for safe food (Herdegen, 2010). This agreement provides for:

[45] See Appendix C with explanations of the different Universal Instruments. The list is by no means complete. This is only an indication of some of the most relevant instruments.

- respect for proportionality (Art. 2.2), which, in the context of research, means balancing and weighing with the aim to ensure that the obstacles to international research activities are not disproportionate to scientific enquiry but with the necessary protection of human, animal and plant life. There must be an appropriate level of sanitary or phytosanitary protection but technical and economic feasibility also need consideration. In a normative sense the principle means to avoid the abuse of rights through a disproportionate allocation of resources (Cottier, 2012: 20, 30).
- the application of "sufficient scientific evidence" (Art. 2.2)
- reference to "international norms, guidelines and recommendations" (Art. 3.1)
- application of recognised methods of risk assessment (Art. 5.1, 5.2), also in research taking into account research activities such as scientific evidence, sampling and testing methods, pest or disease prevalence and environmental conditions (Stanton & Wolf, 2014: 8-10)
- consideration of the available scientific evidence (Art. 5.2) as indicated above. It is important that all sanitary measures are based on scientific evidence and proper risk assessment, disapproving measures that have no rational basis in science. Therefore, provisions that are science-based must be judicially interpreted and applied (Lee *et al.,* 2011: 153).

The WTO international agreements

The WTO international agreements that speak to international trade include *The Agreement on Trade-Related Aspects of Intellectual Property Rights (TRIPS); the Agreement on Technical Barriers to Trade (TBT)* and *the Patent Law Treaty (PTL)* (Journal of International Biotechnology Law, 2009).

- Agreement on Trade-Related Aspects of Intellectual Property Rights

TRIPS recognises the significance of the link between trade and intellectual property and therefore facilitates trade in knowledge and creativity.

- Agreement on Technical Barriers to Trade

TBT must ensure that the standards, technical regulations and assessment procedures are in place to avoid unnecessary obstacles to trade (WTO, n.d.).

- Patent Law Treaty (Journal of International Biotechnology Law, 2009)

PTL was adopted by the World Intellectual Property Organisation (WIPO) and came into force in 2005 with the aim to streamline formal procedures with respect to patent applications on national and regional level to ensure a more user-friendly approach (WIPO, n.d.).

In EBR knowledge of these international agreements is challenging but crucial and EBRECs are confronted with a monitoring obligation to ensure compliance in all research related international trade activities.

4.4.1.3 Human Rights and Social impact control

Human Rights are the basic rights for all human beings and therefore necessitates the need for international regulations to set out the responsibilities, risks and social impact of all research related activities. It prescribes best practice implementation mechanisms. It includes risk assessment with regard to the impacts on local communities and vulnerable low-income countries and encompasses possible project related human rights impacts.

- **UNESCO: Universal Declaration on the Human Genome and Human Rights (1997)**

This universal declaration highlights human genetic techniques that pose risks to values and human rights and it declares unacceptable uses of human genetics. It addresses the principles of autonomy, equality and solidarity and their related rights namely consent, non-discrimination and confidentiality and duties that include the sharing of information and the avoidance of "dangerous" practices (Harmon 2005: 43). This declaration is an attempt to stimulate international research activities and to make role-players aware of the ethical issues of genomic research. It can also be seen as "a first step towards the elaboration of an international biomedical law" (2005: 43).

- **The UN Declaration on the Rights of Indigenous Peoples**

The Declaration on the Rights of Indigenous Peoples of 2007 is a vital United Nations Declaration to account for in many EBR activities. The declaration consists of 46 Articles. The provisions of these articles are framed by, and must therefore be interpreted by the principles of justice, democracy, respect for human rights, equality, non-discrimination, good governance and good faith (UN, 2008). In the context of EBR this implies that research should acknowledge the diversity with regard to languages, cultures and spiritualities. Indigenous peoples and communities are the guardians of biodiversity and the stewards of natural resources. Owing to the exploitation and disparagement of indigenous people and the biopiracy practices of researchers as explained and discussed in Chapter 2, the need for such a declaration was inevitable. The lack of respect under the research community resulted in unethical research practises. The declaration gives the necessary recognition to indigenous

peoples and their right to free prior informed consent as a pre-requisite for any research activity that can affect their natural resources, territories and ancestral lands. The Declaration also voiced good practice activities such as involving the community in the decision-making and the research development processes to increase their sense of engagement and ownership.

Additional relevant declarations to social impact:

- International Declaration on Human Genetic Data (IDHGD)
- Universal Declaration on Bioethics and Human Rights (UDBEHR)
- United Nations Declaration on Human Cloning (UNDHC)

Genetic Research and the sequencing of genomes give way to far-reaching EBR applications. As indicated in the previous chapters genetic data are used for many reasons such as disease prevention or genetic studies, it is used for forensic science and for identification purposes Genetic databank is rising adding to the fear that genetic data will be used for the wrong reasons and infringe on human rights and freedom. These International and Universal declarations are thus an important point of reference in the field of bioethics (Journal of International Biotechnology Law, 2009).

- **Geneva Protocol for the Prohibition of the Use of Asphyxiating, Poisonous or Other Gases and of Bacteriological Methods of Warfare (1925)**

The Geneva Protocol is an international law treaty banning biological weapons and chemical weapons in warfare. This specifically speaks to black biotechnology practices and the use of biotechnology to cause destruction. The safety principle is thus important and should safeguard and ensure the protection of sensitive data that can be used in the development of pathogens or virulent and resistant micro-organisms. The containment principle should prevent unintentional exposure and the release of hazardous organisms.

- **Code of Conduct for Nanotech Research**

The European Commission adopted a Code of Conduct for Responsible Nanosciences and Nanotechnology Research in 2007. This Code of Conduct emerged due to scientific evidence and general fears regarding the risks involved with nanotechnology. However, it is difficult to clearly define such risks and to establish regulation, therefore this code is mainly based on the precautionary principle (Invernizzi, 2010). The Commission acknowledges the gaps in knowledge regarding the impact of this technology on humans, animals and the environment.

The main intention with this code is to protect society from unethical conducts and potential harm but also to maximise the benefits of nanotechnology for society. This Code of Conduct should be adopted for nanotechnology research at research institutions, universities and companies.

EBRECS and researchers in EBR should take note of this Code of Conduct. It provides valuable principles to ensure ethical and safe nanotech research.

The code consists of seven guiding principles:
Meaning: The public should understand the need for Nanotechnology and it should be conducted with the well-being and interest of society in mind. It should respect the fundamental rights of society with regard to the design, the implementation and dissemination as well as use.

Sustainability: Research activities should not harm the environment, plants, animals or people and needs to be safe and ethical. It must also contribute to sustainable development.

Precaution: Nanotechnology research should be conducted according to the precautionary principle. Taking precaution with regard to health, safety and environmental impacts. It must encourage progress but also be proportional to the level of protection and it needs to be for the benefit of the environment and society.

Inclusiveness: The principle of openness is important and must include all stakeholders. There is a need to be transparent to ensure right of access to information and allow for participation in all the decision-making processes.

Excellence: Research integrity is important with the best scientific standards and good laboratory practices.

Innovation: Research governance should encourage innovation and growth, maximum creativity and flexibility.

Accountability: Research organisations and researchers are accountable for the health, social and environmental impact of their research.
(European Commission, 2009)

4.4.2 Biosafety South Africa: Relevant Acts, Regulations and Guidelines.

There are four main regulatory instruments in South Africa that need to be noted in the context of EBR and EBRECs. They are:

- **The Genetically Modified Organisms Act, no 15 of 1997** – This act provides procedures for the responsible application and use of GMOs, focusing on biosafety issues. For EBR and EBRECs in South Africa this act specifically requires that genetically modified organisms do not present hazards to the environment and that there is adequate protection during GMO research activities to prevent accidents and any adverse impacts. EBRECs should do a risk assessment before research may commence.
- **The Environment Conservation Act, No 73 of 1989** – This conservation act provides mandatory requirements of environmental impact assessment for GMOs (Andanda, 2006: 1365). For EBR and EBRECs in South Africa this act specifically requires that the natural environment and ecological communities are protected and preserved. Research activities that are harmful or can damage the environment should not be allowed and researchers should give proof of restoration plans after the research is completed.
- **The Foodstuffs, Cosmetics and Disinfectants (FCD) Act, No. 54 of 1971** – Sets out food safety control measures. For EBR and EBRECs in South Africa this act specifically requires that safety measures are in place for research regarding food, cosmetics and disinfectants. The Higher Education Department (HOD) accepts the Codex Allimentarius guidelines for food safety requirements of GMOs. Under the FCD Act regulation 25 specifically talks to foodstuffs produced through GMOs. EBRECs should be aware of any possible incidental matters that research activities can cause.
- **The National Environmental Management (NEMA) Act No. 107 of 1998** – This environmental management act set out decision-making standards. For EBR and EBRECs in South Africa this act specifically requires the protection of the environment, protecting species, prevent illegal harvesting in research activities, prevent illegal dumping and ensure that the necessary permits and authorisations are in place before the commencement of research activities.

A more comprehensive list with relevant Acts, Regulations and Guidelines specific to the South African context can be found in Appendix D[46] (Andanda, 2006: 1365)

[46] See Appendix D: Biosafety South Africa, relevant Acts, Regulations and Guidelines.

The diversity of national and international documents on biosafety, agricultural, trade and the environment are clearly intended to be mutually complementary, but they need to be carefully interpreted and managed with reference to one another and a healthy measure of goodwill in this will be required to avoid potential conflict. Unfortunately, as they currently stand, these regulations lack coherence, and do not lend themselves to be easily coordinated with a view to effective international collaboration (Journal of International Biotechnology Law, 2009: 177). This situation leaves EBRECs with many challenges, which I will elaborate on in the next section.

4.5 Challenges in complying with statutory responsibilities and the influence on EBRECs

Jane Morris indicates that countries should have a unified approach to biotechnology and biosafety in their national policies, but this is unfortunately not the case in South Africa or any African country. In South Africa, the National Biotechnology Strategy is the responsibility of the Department of Science and Technology (DST) (Morris, 2017: 10). The Department of Agriculture, on the other hand, administers the GMO Act, and in contrast, the Department of Environment Affairs administers the Cartagena Protocol for Biosafety (CPB), the National Environment Management Act (NEMA) and the National Environmental Biodiversity Act (NEMBA).

The different government departments have diverse approaches, leading to ambiguity and confusion, resulting in poor decision-making and regulatory delays (Janssen van Rijsen *et al.,* 2013 as cited in Morris, 2017:10). A case in point is that NEMBA and NEMA can block permits for the release of GMOs, which need to be applied for under the GMO Act. Regulation of GMOs is governed under the GMO Act (Act no. 15, 1997 & Act 23, 2006). All research activities, such as contained use or field trial activities, production (which include general release activities, transport, the import and export as well as any use and application of GMOs falls under the act to ensure that any activity with GMOs in South Africa is conducted to limit the risk to humans, animals and the environment. The GMO Act and the Amendment is thus the regulation that monitors all GMO activities. Different permits are needed relating to the specific activity as indicated above (Biosafety SA, n.d.).

Morris indicates that: “Legislation comprises not only an approved Act governing biosafety, but also associated Regulations and Guidelines” (2017: 10). The approach outlined in the policy should be in alignment with regulations and the wording of the act. The concern of Morris is that without an appointed body to administer legislation, the biosafety legislation is meaningless (2017: 11).

The lack of coherence also directly influences the decision-making process of EBRECs and the researcher's code of practice. Catherine Rhodes explains this complicated scenario with the following concerns and examples (Rhodes, 2009: 177–199):

1. A lack of clarity about what rules to follow and what is applicable. The lack of coherence makes adherence to the law unclear, which is illustrated in the following example. In a case where a genetically engineered bacterium needs to be exported, for instance, it may be unclear whether to apply rules on trade or regulations on conservation of biodiversity, or a combination of some or all the regulations. The problem is a lack of referencing between rules and regulations. The Cartagena Protocol also does not cover the LMOs addressed by other agreements (Article 5) and does not indicate the specific agreements relevant to this exclusion. States may accordingly be unaware of rules they should apply or the rules that other states will use.
2. Contradictory Provisions in regulations make it unclear whether rules apply and affect predictable behaviour or possible expectations. Only if all governments follow the same rules will they know what to expect from one another. The treatment of GMOs is an excellent example of how the Cartagena Protocol rules regarding the import of GMOs conflict with the rules of the WTO Agreement (Joyner, 2005: 15). National policies also required a unified approach to biotechnology and biosafety. In South Africa, various approaches within different government departments lead to uncertainty, regulatory delays and poor decision-making practices. The Department of Science and Technology is responsible for the National Biotechnology Strategy, while the GMO Act is handled by the Department of Agriculture (Morris, 2014: 10). This is a case where one department can have a positive approach to biotechnology development while another adopts an opposing view.[47]
3. Overlap of Provisions. The development of regulation over time and separately from each other, resulted in overlapping areas and duplication of efforts. For instance, scientific knowledge can be provided for under the benefit-sharing provisions of the International Treaty on Plant Genetic Resources (Articles 8 and 13), but the same knowledge can fall under the benefit-sharing provisions of the Bonn Guidelines, or even under the technical assistance provisions of the Plant Protection Convention (Article XX). This duplication creates perplexity and undermines efficiency (Joyner, 2005: 20).

[47] If GMO research is conducted under NEMA, and the Department of Science and Technology conduct an environmental impact assessment and the outcome is that the particular activity is acceptable, the Department of Agriculture who manage the GMO Act nonetheless retains as the authority the final decision to grant a permit (Biosafety SA, n.d.).

4. Prohibitions – Lack of Clarity. In some cases, the regulation allows a particular action, whereas other regulations or laws prohibit the same action. An example is a case where the UNESCO *Declaration on the Human Genome and Human Rights* allow therapeutic human cloning[48] under strict conditions (Article 11). The UNESCO rule, however, forbids *reproductive cloning*. On the other hand, the United Nations General Assembly approved a declaration in 2005 that prohibits all forms of cloning, including reproductive and therapeutic cloning (Rhodes, 2009: 190).
5. Different dispute settlement mechanisms, furthermore, make the resolution of a conflict difficult. It could create a scenario where one body makes a ruling directly in contradiction of another regulation's provisions or principles. If there is a dispute on intellectual property rights and genetically engineered plants, for instance, the question can be asked who should deal with it? The WTO under Article 64 of the TRIPS Agreement (*Trade-Related Aspects of Intellectual Property Rights Agreement)* or will it be dealt with according to the *International Treaty on Plant Genetic Resouces* (Article 22) or perhaps procedures from national guidelines? (Journal of International Biotechnology Law, 2009).

These examples clearly show why Rhodes (2009: 177–199) argues that the regulatory framework's lack of coherence creates problems to control biotechnology practices effectively. Similarly, Pamela Andanda, from the University of the Witwatersrand, points out that biotechnology regulations have not been effectively developed in Africa and are often "splintered" (Andanda, 2006: 1361). She also indicates that it is not easy to regulate EBR or biotechnology because it is such a dynamic field (ibid, 2006: 1368).

4.6 The role of ethics and principles in a regulatory framework

Despite the concerns raised above regarding regulatory frameworks, many national and international laws are in place and need to be considered and obeyed in the research process. The question is, how and where do ethical principles fit into the legislative and regulatory framework? My response to this question is that there is a very close relationship between EBR ethics and applicable laws (Australian Law Reform Commission, 2010: 6.60). Saunders and Komesaroff (2010: 6.60) pointed to the relationship between ethics and law when they suggested that: "the law should focus on the settings in which individuals engage in ethical decision making and seek to ensure that it is open and free from coercion and that adequate information is provided to allow individuals to make their own decisions after full and careful reflection". In addition, they indicated: "the integrity of researchers, and indeed of any

[48] Therapeutic human cloning is where stem cells are produced for therapeutic uses.

decision-makers in a regulatory environment, should be assessed by reference to the ethical values and principles on which that framework is based" (ibid: 2010: 6.63).

Thus, research ethics is an implementation of, and a commitment to, the values and principles that operate to maintain the consistency and coherence of the ethically founded regulatory framework. The commitment is based on the understanding and awareness of ethical principles, which is understood to guide, promote and justify good conduct and decisions in EBR. But the most important role of ethics in a regulatory framework is justification, because ethics is all about choices, responsible choices. Such decisions or choices can only be justified, though, when they are based on sound moral reasoning, when they are impartial, and overriding self-interest considerations, promoting human well-being and being non-arbitrary (Komesaroff, 2010: 6.64–6.65)

Making ethical choices in EBR means judiciously weighing the relevant considerations identified by principles. Thus, good moral judgement in an EBREC will mean that all aspects need to be considered, and moral principles must reasonably support a decision (ibid: 2010: 6.66). In this way, ethics can justify the formation of a regulatory framework and appropriate principles to guide, promote and justify decisions.

The following section deals with the existing ethical principles and the possible lacunae in the perplexing environment of EBR and decision-making in EBRECs.

4.7 Existing ethical principles and lacunae

4.7.1 Existing Principles: A summary

It is important to differentiate between principles and values before the existing principles in EBR can be outlined and discussed. Ethical principles are universal rules that are permanent and unchanging, but values can change with time and are subjective. Principles, therefore, influence and inform values (Weis, 2014).

Principles are grounded in specific approaches, such as utilitarianism, where the principle holds the greatest good or the benefits for the greatest number of people, also considered the cost vs benefit principle. The universalism approach considers norms that apply to all cultures, and deals with respect and fairness and that ethical principles speak to everybody. That means any obligation, rights or a list of virtues is for everybody and not merely for some (O'Neill, 2002). Additionally, if ethical principles speak to everybody it will also recommend or prescribe the same to everybody. If we think of human rights the universal approach will not only emphasise rights for all humans but also that they have the same rights. According to O'Neill, principles can guide action and at the same time allow flexible interpretation (O'Neill, 2002).

Some principles are grounded in legal and moral rights. The justice principle can be summarised by answering the following questions: 1) is it fair? 2) is it right? 3) who gets hurt? 4) who or what pays the consequences? 5) who takes responsibility for the consequences?

Professor Gillon from Imperial College in London argues that the four biomedical principles of *autonomy, non-maleficence, beneficence and justice* can be used alone or in combination to explain or justify ethical issues and that it is compatible with a wide variety of approaches or moral theories (Gillon, 2003: 307). He also stated that it justifies all universal and substantive moral norms in medical ethics and ethics in general (2003: 308). According to Gillon, these four principles also help to avoid moral imperialism (to imply it is the only correct way of doing ethics) and moral relativism (any ethics will do) (2003: 309). Professor Macklin from the Albert Einstein College of Medicine in New York agrees with Gillon that the four principles approach is a valuable and sound way to analyse any moral dilemma. But Macklin includes and emphasises the precautionary principle (PP) as well (Macklin, 2003: 275). Adopted in the Convention on Biological Diversity (CPB) and framed as Principle 15 of the Rio Declaration (*United Nations Conference on Environment and Development (UNCED*), 1992, the PP states: “Where there are threats of serious or irreversible damage, lack of full scientific certainty shall not be used as a reason for postponing cost-effective measures to prevent environmental degradation” (Morris, 2017: 7).

Similarly, Meslin and Cho reason that the current general framework for ethics in EBR seems to be based on the precautionary principle and protectionism, greater transparency and public involvement in the scientific processes (Meslin & Cho, 2010: 379). In the natural or environmental sciences, the PP can be seen as a broad epistemological and legal approach to prevent harm in cases of uncertainty. The PP is indicated as the most important, well-known principle in scientific research. It becomes a rationale for many international declarations in different fields, such as environmental protection, sustainable development, etc. It also attracted arguments and debates on how it is defined and applied to complex scenarios with multiple risk factors. In the EU, the precautionary principle is a statutory requirement by law in certain areas.

The PP is defined in many ways, e.g. “caution in advance” or caution practised in the context of uncertainty (Jordan & O'Riordan, 2004: 34). Therefore, it can be argued that it is indeed a widely accepted principle that can be applied in many different fields and research areas. However, the PP is also a much debated and controversial principle. Crozier and Schulte-Hostedde argue that the precautionary principle creates challenges and could be problematic in some research studies. The example they use to prove their point is a study where the effects of an environmental pollutant need to be tested on a rare but not endangered

amphibian species to determine the danger to that species. Doing this kind of study can mean that many amphibians are exposed to the toxin, but the research can save the species from extinction in the long term. Crozier and Schulte-Hostedde, however, argue that the Precautionary Principle will probably disapprove of the study due to the potential harm to the amphibians, and advocate for a different approach based on six principles[49] that they claim provide for a more collective ethical reflection of research studies (Crozier & Schulte-Hostedde, 2015: 578).

There are different ideas and versions of the PP in the literature. Selgelid talks about a weak, a moderate and a strong version (Selgelid, 2016: 946). Applying the weak version as adopted in the Rio Declaration on Environmental Development is considered relatively inefficient because it does not imply a high degree of risk aversion. It indicates that precautions should be taken when there are threats of irreversible or severe damage or scientific uncertainty, and environmental degradation should be avoided. This version thus justifies preventative action against potential dangers.

Stronger and moderate versions are more clearly risk-averse and indicate that no action should be taken that pose serious dangers. Moderate versions hold that actions should be withheld “if the dangers they pose are not merely serious but exceed severity thresholds” (2016: 946). However, Cass Sunstein, a professor at the University of Chicago, argues that the stronger version is incoherent because profound implications could happen in any course of action. He indicates that the strongest version of the principle will prohibit all development and release of GMOs, because they can pose uncertain dangers in the environmental context. However, as Sunstein points out, the failure to develop and release certain GMOs might also pose a serious problem, because not using GMO development can cause major famine. He even concludes that the use of the principle is useless due to its incoherent nature (Sunstein, 2005: 24–32).

Sunstein's argument is in contrast with Gloria Origgi and many others like David Resnik, who defend the PP against the criticism mentioned above. Origgi argues that the PP is an ethical, normative principle that helps us deal with the complexity and interconnections of our natural and social system, it makes us aware of catastrophic outcomes. It makes us more responsible and robust to possible risks (Origgi, 2014: 11,12). David Resnik appeals to the PP with the following statement: "the basic idea of the precautionary principle is that we should take

[49] The six principles of Crozier and Schulte-Hostedde: Freedom, Fairness, Wellbeing (for human entities) and Replacement, Reduction and Refinement (for sustainability)

reasonable measures to avoid, minimise or mitigate harms that are plausible and serious" (as cited in Selgelid, 2016: 947).

Despite these concerns, different opinions and definitions, I will argue that the PP should be a fundamental concept/principle in environmental and biosafety research ethics. UNESCO formulated the following description in 2005 that speaks to Resnik's approach as previously mentioned: "When human [scientific] activities may lead to morally unacceptable harm that is scientifically plausible but uncertain, actions shall be taken to avoid or diminish harm." (UNESCO COMEST, 2005: 49). Under this understanding, the PP is a constitutional principle that is built in some legislation to protect human rights. This principle indicates that there should be a reasonable balance between an activity and its consequences.

Moving on from the PP as a constitutive principle of EBREC reviews, it is important to also consider other principles that have received traction in international circles and are widely supported. The European Commission, for instance, indicated in the *Stakeholders Acting Together on the Ethical Impact Assessment of Research and Innovation* (SATORI) project the need to refer to more general ethical frameworks because specific ethical frameworks for the discussed disciplines are not well developed. The project aimed to develop standard best practices for ethical assessment and develop common approaches and a suitable framework.

According to Texas State University, the primary Biosafety principle is *containment*, which refers to different safety methods for managing infectious agents in the laboratory and eliminating or reducing environmental and human exposure to potentially harmful agents external to the laboratory (Texas State University, 2014).

The European Commission promotes ethical conduct in research and innovation, and the maintenance of integrity in all actions. SATORI indicates that the predominant emphasis in EBR should be the following:

- "Advance the welfare of society, particularly in the fields of health, safety and the environment."
- "Advocate suitable precautions against possible harmful side-effects of science and technology" (SATORI, 2015: 8).

Through the SATORI project, the European Commission declared that "ethics is given the highest priority in EU funded research" (Rodrigues, 2019). The SATORI policy also states that legal frameworks should support ethics assessment.

The project stakeholders, however, acknowledged the difficulties with creating a global framework, mentioning the following obstacles: differences between ethical values and

philosophies, countries and cultures, and scientific fields. As a result, SATORI provides and proposes a broad framework for ethical principles and issues. They provide two sets of ethical principles, 1) a set that applies to all types of research and 2) a set that applies to specific research fields, including natural sciences, life sciences, medical sciences, engineering sciences, social sciences and computer and information sciences.

In the SATORI[50] project the following ethical principles are indicated:

A. General Ethical Principles and Issues for all Types of Research:

- "Research Integrity
- Social Responsibility
- Avoidance of and openness about potential conflicts of interest
- Protection of and respect for human research participants
- Protection of and respect for animals used in research
- Protection and management of data
- Protection of researchers and the research environment
- Dissemination of research results" (SATORI, 2017: 11).

B. Additional Field-specific Principles for Research:

1. <u>The Natural Sciences</u>

- "Take special precautions to ensure that researchers and staff involved in conducting the research are not exposed to serious physical harm or strain as a result of working with harmful biological, chemical, radiological, nuclear, or explosive materials;
- Take special precautions to minimise any potential harm to the environment, animals, or plants caused by the use of harmful biological, chemical, radiological, nuclear, or explosive materials during the research;
- Consider whether the results of the research might have military applications, and whether the results of the research might contribute to the proliferation of weapons of mass destruction;
- Take special precautions to prevent or counter the effects of potential misuse of security-sensitive chemical, radiological, or nuclear materials and knowledge (e.g., the appointment of a security advisor, limiting dissemination of the research results, and staff training)" (SATORI, 2017: 11–12).

[50] The principles as discussed in this section have been taken verbatim from the SATORI (2017) project and is available from the source for further consultation.

The principles indicated above for the natural science are, importantly, all based on a precautionary approach.

2. The Engineering Sciences and Technological Innovations

- "Ensure that the technology to be developed does not pose risks of harm to public health and safety in terms of both its production and societal use;
- Ensure that the technology does not harm, or pose inherent risks to, individual freedom, autonomy, and privacy, human dignity or bodily integrity, as well as the well-being and interests of individuals and groups;
- Anticipate potential risks and harms to the environment resulting from the uses of the technology, and ensure the prevention of environmental harms caused by the use of bio-chemical, radiological and explosive materials;
- Ensure that the technology does not pose any unnecessary risks of harm to animals;
- Ensure that researchers and staff involved in research and development are not exposed to physical harm resulting from harmful biological, chemical, radiological, nuclear, or explosive materials;
- Anticipate and avoid the dual-use (e.g. for military purposes) or misuse of the technology" (SATORI, 2017: 12–13).

The principles indicated here for Engineering Sciences and Technological Innovations are based on the prevention of harm and risk assessment principles.

3. The Life Sciences

- "Ensure that the research, regardless of its potential applications, does not pose any direct or long-term risks of harm to public health and safety (e.g., by taking adequate precautionary measures against accidental release of hazardous biological agents);
- Consider how the research might lead to innovations that could harm human and civil rights, interests or the well-being of individuals and groups in society, or the common good, and how the research and innovation activity might be directed to enhance rights, well-being and the common good;
- Anticipate, assess and communicate how the research and innovations based on this research might pose risks to or harm biodiversity, the integrity of natural ecosystems, and the welfare of animals;
- Consider concerns about naturalness (authentic generation by nature without human interference) in relation to research into animal and plant breeding, cloning, and the (genetic) modification of biological organisms;

- Ensure that researchers and staff involved in conducting the research are not exposed to serious physical harm resulting from working with harmful biological, chemical, or radiological materials;
- Consider whether the research results might have military applications;
- Prevent or counter the effects of the potential misuse of security-sensitive biological, chemical, or radiological materials or knowledge (e.g., through the appointment of a security advisor, limitation of dissemination of the research results, staff training)" (SATORI, 2017: 12–13).

Principles indicated above by SATORI for the Life Science are also based on prevention of harm, risk mitigation and the prevention of misuse or dual-use applications and a precautionary approach.

4. <u>The Computer & Information Sciences</u>

- "Ensure that new research and innovations offer reasonable protection against any potential unauthorised disclosure, manipulation or deletion of information and against potential breaches of data security (e.g., protection against hacking, denial of service attacks, cracking, cyber vandalism, software piracy, computer fraud, ransom attacks, disruption of service);
- Ensure that new research concepts and innovations do not pose any unjustified inherent risks to the right of individuals to control the disclosure of their personal data;
- Ensure respect for freedom of expression, intellectual property rights, and other individual rights and liberties;
- Consider how new research concepts and innovations might harbour or counter unjust bias in terms of age, gender, sexual orientation, social class, race, ethnicity, religion or disability;
- Consider how the research or innovation activity might harm or promote the general well-being of individuals and groups in society (e.g., effects on the quality of work or quality of life), the common good, and environmental sustainability;
- Consider whether the research in computer and information sciences, and innovations in ICTs might have military applications" (SATORI, 2017: 13).

The SATORI principles with regard to Computer and Information Sciences can broadly be classified as prevention of harm or protection against harm, risk mitigation, respect, and prevention against dual-use (misuse).

5. The Medical Sciences[51]

- "Adhere to rules and regulations concerning public health and safety, and those concerning the use of stem cells and tissues in medical research;
- Have consideration for concerns about the commodification of life in relation to (aspects of) human genetics research and human reproductive technologies" (SATORI, 2017: 12).

It is interesting and important to note that the approach of SATORI may be different for the various disciplines, but the overarching ethical principles seem to be the same. This confirms the importance of general principles as the basis for REC reviews in general, and the reviews of EBRECs in particular. This is also confirmed by most of the research institutions in Europe: they all have a code of conduct for the research conducted in their ambit, and in that they all broadly follow the internationally accepted ethical principles, albeit with variations tailored to their specific situations. An example is the European Organization for Nuclear Research (CERN) who aims for a domain-specific ethics. The principles they stand for, however, are the well-established ones of scientific integrity, responsibility towards society and professional obligation.

Similarly the Società Chimica Italiana compiled a "Charter of Ethical Principles for the Chemical Sciences" with general ethical principles adopted from national and international chemistry societies:

- "opposition to the improper use of chemistry"
- "safeguarding of the environment and its ecosystems"
- "improving the quality of life without harming the world around us"
- "dissemination of awareness of the advantages and benefits of the chemical sciences in public opinion" (SATORI, 2015: 25).

As has been noted in the previous paragraphs, these principles for the Chemical Sciences also serve to address the prevention of harm, non-maleficence and beneficence (which incorporate benefit vs harm principles).

The Charter furthermore acknowledges *"conceptual dualism",* in the sense of the tension that exists between the aim to formulate and adhere to universally shared principles, and the values each and every individual brings with them to the conversation, coming from their

[51] Only applicable EBR principles in the Medical Sciences were selected and not the full SATORI list. The section for Social Sciences is not included as it is not applicable for the purpose of this thesis.

upbringing and context. Formulated in its own words, the Charter summarised this tension as follows:

> Each individual's general ethical principles belong to their upbringing and the country's traditions in which they live. Culture, Morality, Ideology and Religion exert considerable influence over individual behaviour and differences among nations are significant. A General Charter of Ethical Principles for the Chemical Sciences must consider such differences and put forward principles that can be universally shared (2015: 25).

This focus on general principles is also shared in France, where scientific research is regulated by the French National Research Agency (ANR). The ANR established an ethics framework in 2014 regarding scientific integrity and ethics policy, and in 2009 the ANR's 2009 code of ethics singled out the following principles that should guide research: *objectivity, selflessness, respect for information, confidentiality* and the *prevention of conflict of interest* (SATORI, 2015: 21).

In similar efforts, biologists of North America and Europe collaborated to create a framework for ethical and responsible research in their field. Some universal principles were shared, but there were also differences in the frameworks they eventually developed. The American version is more proactive, while the European version is more restrictive. The American version included "*respect for the environment and tinkering"*. Meaning that the environment should be repaired or improved. The universal principles they appealed to include *transparency, open access, safety, education and peaceful purposes*. The European version, in turn, included the general principles of *modesty, community concerns and honest responses, respect, responsibility and accountability*.

Other initiatives to articulate a framework for ethical research in the ecological sciences include that of the Canadian researchers Crozier and Schulte-Hostedde who suggested six principles, three covering human entities and the other three non-human entities. According to them, these six principles address all ethical concerns in ecological research. The first three are *freedom, fairness and well-being*, which, according to them, are derived from Beauchamp and Childress (1977). Freedom was derived from *"respect for autonomy",* fairness was derived from *"respect for justice"*, and well-being was derived from *"respect for beneficence and non-maleficence"*. These three principles also cover compliance and all ethical implications for human entities such as communities and conservation gatekeepers, an important consideration in EBR (Crozier & Schulte-Hostedde, 2015: 585–586). The other three values Crozier and Schulte-Hostedde promote are *replacement, reduction and refinement*, similar to the 3Rs Principle for Animal Ethics, but applied in Environmental Ethics to lower the ecological footprint and act as a *sustainability principle* (2015: 586).

- Replacing unsustainable materials;
- Reducing the use of resources; and
- Refining practices to develop a positive environmental balance (Crozier & Schulte-Hostedde, 2015: 585).

Crozier and Schulte-Hostedde (2015) posited that an ethics strategy and direction must consider the evolving needs of the ecological (environmental) research community. The escalation of environmental issues such as climate change, pollution and many other destructive anthropogenic phenomena need to be addressed and monitored by researchers in environmental sciences through innovative research methods (Minteer & Collins, 2008). To empower researchers in their task, they need clear ethical guidelines and strategies. While ecological research mainly focuses on relationships and the environment of organisms, they indicated that field studies and experiments have various ethical implications because they have most often impacted the ecosystem and local communities; however, even observational studies can have a negative effect. [52]

On the other side of the Earth, India has also developed a regulatory framework for ethical research in the EBR domain, and then a strict one for that matter, making provision for safety measures and regulations for biosafety and biosecurity. This was done in 2002 by the India Department of Biotechnology, formulating the "Ethical Policies on Human Genome, Genetic Research and Service" (Gandhi, 2015: 13).

The following principles govern their code of conduct for research:

- **"Non-maleficence** – to ensure that discoveries of biomedical research and knowledge generated do no harm, and that bio-science and biotechnology discoveries do not facilitate bio-terror/bio-warfare.
- **Beneficence** – to ensure that the scientific knowledge gained through life sciences research benefits the society that outweighs the risks and harms.
- **Principles of institutional arrangement** – to ensure that all procedures comply and all institutional arrangements assure bio-security. Access to biological agents is allowed to bona fide scientists in a transparent manner.

[52] The following example from Canadian ecological researchers serves as an example. A very successful long-term study in the Canadian Rocky Mountains on a population of bighorn sheep has been studied for many years. The research team has incredibly detailed data about the phenotype, life-history and pedigree of marked individuals in the sheep population. Many scientists, postgraduate students and postdoctoral fellows studied the population that leads to many important publications. Unfortunately, a cougar recently started chasing and killing all of them and drastically reduced the sample size of the study. In this region it is legal to hunt cougars and therefore the team could consider killing the cougar but also needs to consider that they could kill the wrong cougar (Crozier & Schulte-Hostedde, 2015: 578).

- **Principles of risk minimisation** – to ensure care and caution is taken to restrict the dissemination of dual-use in cases of severe risk that information or knowledge could be readily misused to inflict harm through bioterrorism or bio-warfare.
- **Principle of ethical review** – to ensure that research activities are subjected to ethics and safety reviews and monitoring to establish their ethical acceptability.
- **Principles of transmission** – of ethical values, whereby the duties and obligations embodied in the code are transmitted faithfully to all who are or may become engaged in the conduct of research.
- **Principles of voluntariness** – whereby researchers are fully apprised of the research and the impact and risk, but retain the right to abstain from further participation in research that they consider ethically or morally objectionable.
- **Principles of compliance** – to abide by laws and regulations that apply to the conduct of scientists, duties and obligations embodied in this code and disseminate the same to all concerned" (Gandhi, 2015: 12–13).

Again, we see in this code the same general approach followed, with more or less the same general principles articulated, only in different words and formulation, with additional information added to make provision for the specific country context. However, the general meaning and results of the code aim for the same outcome that of other similar codes articulated in other parts of the world.

In Malaysia, modern biotechnology has given rise to some controversies and ethical issues,[53] prompting them to also introduce, in tandem with western countries, ethical guidelines for modern biotechnology, acknowledging the need for suitable guiding principles. They proposed that the four key biomedical principles be re-organised into the following three principles: *autonomy and public interest; beneficence and non-maleficence*; and *justice and non-discrimination* (Hasim *et al.,* 2019: 57).

In Australia, the ASTEC Working Group developed principles and guidelines for "Ethical Conduct of Research in Protected and Environmentally Sensitive Areas" (ASTEC, 1998: 72). They acknowledged the interdependent relationship between natural sciences and protected areas, as well as community values, and an efficient and transparent ethical approval process.

[53] An example of these issues is the ethical concerns of the Muslims in the Klang Valley region of Malaysia of genetically modified rice containing an animal gene. The ethical issues and concerns are therefore about the "risk to human health, the threat to natural order of living things, market monopoly by giant companies and developed countries, the wrongness in modifying living things and confidence in government regulation" (Amin *et al.,* 2013: 359).

The principles they identified as their point of departure in this regard were: *conservation, transparency, indigenous-, community- and peoples' concern.*

Additionally, ASTEC included principles relating to the Role of Governments regarding biodiversity and international environmental obligations, and then also added Administrative principles. Importantly, the ASTEC Working Group indicated that the overriding principle that should guide research in protected and environmentally sensitive areas is the *Precautionary Principle* (1998: 72).

Another initiative came from The Gene Technology Ethics Committee of Australia, which published a National Framework for the Development of Ethical Principles in Gene Technology in 2006. This framework was necessary to provide scientists in gene technology a national reference point for ethical consideration by developing applicable ethical principles when working with GMOs and GMO products, considering environmental and other relevant gene technology issues. (Gene Technology Ethics Committee, 2006: 5). Nine principles to cover the most important ethical issues were proposed, which can be summarised to advocate the following canonical principles: *integrity, responsibility*, *minimise risk, prevent harm, respect, protection, justice, non-maleficence and beneficence.*

Insofar as EBR also ventures into themes related to responding to the challenges of climate change, the UNESCO *Declaration on Ethical Principles in Relation to Climate Change* of 2017 is also of relevance to this discussion (UNESCO, 2017). In this Declaration six ethical principles are articulated: *Prevention of harm, Precautionary approach, Equity and justice, Sustainable development, Solidarity, Scientific knowledge and integrity in decision-making.*

The World Commission on the Ethics of Scientific Knowledge and Technology of UNESCO (COMEST) proposed an ethical framework for robotics ethics in 2017 with the following ethical principles at its core: *human dignity, autonomy, privacy, do no harm principle, responsibility, beneficence,* and *justice* (UNESCO, 2017). These UNESCO principles in the different disciplines are again built on and add to the canonical principles of bioethics that we are familiar with at this point in the thesis.

When research only concerns environmental ethics, Diana-Abasi Ibanga from the University of Calabar in Nigeria promotes a slightly different approach and identifies five principles for African Environmental Ethics. He indicates that it should guide peoples' behaviour regarding the environment and function as a predictive sense, (meaning to make them aware of what could happen in future, for example, adverse effects), before acting. Ibanga also suggests that the proposed principles should guide researchers in African environmental research (Ibanga, 2018:126). The principles that Ibanga identifies are the following:

- "Principle of Accommodation – meaning that daily decisions and actions need to consider and accommodate all non-human existence and generations to come.
- Principle of Gratitude – actions need to reflect gratitude towards human and non-human existence because they support your life.
- Principle of Restoration – to restore nature after an act of destruction, e.g. to re-plant trees that were cut.
- Principle of Control – to control actions of negative consequences to society and nature.
- Principle of Necessity – only act on necessary decisions and actions" (Ibanga, 2018:126).

Ibanga's main idea is that research activities should help communities to provide human needs, but to do so in a manner that posterity and the integrity of the ecosphere are safeguarded and not placed at risk. Ibanga's approach can be interpreted as support for the canonical principles of *research integrity, respect, protection, restoration, prevention of harm,* and *justice.*

Ibanga's contribution also helps to formulate the insight that differences in culture are the main reason for different research ethics views, giving rise to other, creative ways of applying certain principles – for example, individual consent is a principle that is typically emphasized in Western societies, versus society or community consent, which is emphasized more in African societies. Further problems, however, emerge when research frameworks need to be practically implemented in individual African countries.[54] Due to the lack of research infrastructure in many African countries, and perhaps due to an authoritarian regime, informed consent is often not formally required (Weinbaum, 2019: 46), opening the door for the dubious practice of ethical dumping that was described above in Chapter 3.

The way research activities are defined may also differ from society to society, or context to context: with privacy-sensitive information and data protection a case in point, the definition in Europe being quite expansive, while a much narrower definition is used in the US (Wienbaum, 2019:45).

Similarly, the European Commission indicated that they would not fund research that modifies genetic heritage, entails human cloning, or involves stem-cell procurement. On the contrary, EU member countries have different laws regarding the examples mentioned above, allowing this research. On the other hand, China does not hold ethical or religious beliefs against

[54] Hariadi (2015: 139) in contrast, identified sustainability, proportionality and responsibility for the cause as three principles of environmental ethics that should guide environmental and ecological research.

certain controversial research, such as embryonic stem cell research. As such, these cultural and national differences will have to be incorporated somehow in the review processes of EBRECs, pointing into the direction of difficult meta-ethical conversations between members of EBRECs on the meaning of principles in general, and the interpretation of the principle of *respect for cultural and political differences* in particular.

Another approach to acknowledging cultural differences has been followed by the TRUST Project,[55] which aims to create research standards worldwide. They created a Code of Conduct for Research in Resource-Poor Settings in 2017, and also developed the San Code of Ethics to prevent the exploitation of the vulnerable San People of Southern Africa. It is important to note though, that in spite of this unique approach to drafting it, the San Code of Ethics also promote the well-known canonical principles that include: *respect, honesty, care, justice and fairness.* (TRUST, 2017).

To conclude then: acknowledging the extensive and multidisciplinary field of EBR, as well as the fragmented international efforts to delineate frameworks and principles for ethical EBR as indicated in the previous sections, it is evident that identifying a final or comprehensive set of ethical principles is not an easy task. What is then the way forward? In the following section I will start to articulate a proposal for a possible way forward, just mentioning it, and exploring it further in my last, concluding chapter

4.7.2 Is there a way forward then?

A universal problem with EBR ethics assessment is that nothing, or very little of it is institutionalised, with no formal standards or ethical training, there is no formally prescribed procedure for reviews, or a systematic way of thinking about the ethical issues involved. It all happens more or less on an informal basis with a lack of direction and guiding principles (SATORI, 2015: 27).

The *International Journal of Sustainable Development and World Ecology* (1999: 79) emphasises that ethical criteria for research must not be derived empirically but rather culturally but this would mean, consequently, that these ethical criteria are prone to change (or interpretation) according to circumstances and time. Furthermore, controversial issues can engender many different views, even in a sophisticated, informed life-sciences community. Despite the amorphous nature of ethical problems in the wide spectrum of EBR, a "single issue", for example GMOs, will always raise many different social questions, depending on a variety of "points of departure". Instead of just mirroring this diversity, my contention is that

[55] The TRUST project is a global Code of Conduct. The project received funding from the European Union and aims to achieve partnerships in research. The code is designed to combat ethics dumping and to guide researchers from all disciplines.

EBRECs should respond to this reality with processes of informed discussion (1999: 80) evoking the canonical principles referred to above as guides and prompts, and lifting deliberations above subject-specific discussions and principles with a view to addressing and serving societal needs for biosafety and environmental integrity.

As a result of my research and my attention to discussions within the research community, and based on the current state of ethical principles in EBR, I conclude that the lack of a well-designed set of principles is a challenge for EBRECs. Existing principles tend to speak to scenarios within a discipline, or to a particular discipline only. Another drawback is the use of long lists of confound principles, difficult to decode, interpret or to remember. With this situation in mind and the multidisciplinary and complex nature of EBR, I identified four categories of principles, which I want to call **MSLS**, that I would like to propose as a framework that can be used fruitfully and effectively by EBRECs:

1) Principles as a **M**oral Concept
2) Principles as a **S**ocial Concept
3) Principles as a **L**egal Concept
4) Principles as a **S**afety Concept

The last chapter will cover and explain my proposal and allow me to evaluate it for further discussion.

4.8 Conclusion

The research questions that I tackled in this chapter were: *What is the current state of ethical principles for ethics reviews in the field of environmental and biosafety research ethics? Which principles are currently used in this context, and how? What are the shortcomings of the current principles, and how can they be overcome?*

The chapter started with a comparison between two assessment approaches, principles vs casuistry. International frameworks and universal codes were then investigated and discussed. The national and international legislation, regulations, protocols, and studies regarding EBR were listed and considered to enlighten the current state of principles in research ethics in this multidisciplinary field. Comparing principles and frameworks in the different disciplines revealed that certain ethical principles are accepted as universal across areas. Other principles are more discipline specific. In EBR, the principles that support a cautious approach apparently receive priority, as well as principles that support social justice, emphasising public needs and reciprocity.

The next and final chapter of this study will answer the last research question: *What ethical principles need to be adopted by EBRECs and should guide them in their decision-making.* I concluded this chapter with a proposal of four broad categories of principles that should be articulated with a view to guiding EBRECs. The last chapter will discuss the recommended categories and principles that can serve as an easy guide for South African EBRECs. In my last chapter I will also identify themes that need to be further investigated in order to address the current gaps in the frameworks and principles for EBRECs.

CHAPTER 5: SUMMARY OF FINDINGS, CONCLUSION, RECOMMENDATIONS AND SUGGESTIONS FOR FURTHER RESEARCH

5.1 Introduction

This study identified lacunae in the scholarly literature on the theme of a global and uniform set of principles for EBR. There is this existing gap, despite widely expressed concerns about innovative research in biotechnology and related fields. The study also highlighted the controversies of biotechnological initiatives in EBR and the need for well-defined principles to guide EBRECs.

Against the background of my introductory chapter I concentrated in Chapters 2 and 3 on my supporting questions to set the scene for the study and determine what EBR ethics in action means and what the relations are between environmental and biosafety ethics.

In Chapter 4, I elaborated on the current state and application of principles in the functional areas typically covered by EBRECs. In this chapter I also touched on the national and international frameworks, legislation and declarations that could accentuate the principles that could be used to guide EBRECs.

This fifth and final chapter will round off by first returning to the research questions and briefly discussing how they were answered. This chapter will also discuss the recommended categories and principles applicable to EBRECs in the South African contexts. I will then conclude with suggestions for implementation and themes for further research.

5.2 Reflection on the research questions

The previous chapter thoroughly discussed my first and second research questions regarding the state of ethical principles in EBR and the shortcomings of the currently available principles. In this chapter I will unpack my response to my final research question, which is: *What ethical principles need to be adopted by environmental and biosafety research ethics committees and should guide them in their decision making?* I do so in terms of identifying and elaborating a suitable ethical framework with principles that can guide all EBR activities as well as the review processes of EBRECs.

The contributors to the Stakeholders Acting Together on the Ethical Impact Assessment of Research and Innovation (SATORI) project identified three challenges regarding developing a globally accepted framework for EBR. The first is the differences between countries and scientific fields, making it difficult to harmonise ethical principles and scientific fields. The second is to ensure a framework that functions on a general and aspirational level and

provides the necessary tools to solve concrete ethical dilemmas. The third and possibly the biggest challenge is to achieve a national and global acceptance for the framework (Jansen, *et al.,* 2017: 9–10).

While there is a diversity of ethical traditions influencing global moral ideas and codes of conduct, at the same time there is a worldwide agreement on the importance of ethical principles to ensure responsible and accountable environmental and biosafety research. But, there is also a lack of generally accepted strategies and methods to identify, articulate and implement these principles. Accordingly, my challenge with this thesis was thus to provide a solution for EBRECs, at least in the South African context, learning about the complexity and controversies around EBR from my discussions in Chapters 2 and 3 where my focus fell on the nature and scope of biosafety and environmental research in action.

In my investigation, to answer my first research question regarding principles currently in use, I could identify three broad categories of principles: principles dealing with ethical scientific integrity; principles dealing with ethical conduct in research and principles dealing with the ethical treatment of participants and/or the environment. I also developed a good understanding of the manner in which cultural differences, different disciplines and the specific ethical challenge of a case will determine the application of possible identifiable ethical principles in EBR.

I am well aware, though, of the enormity of the task to develop a list of well-articulated and globally accepted principles for environmental and biosafety research ethics for EBR and EBRECs, and even if there is a dire need for such a framework (ASSAf 2015: 28), I am also well aware of the fact that such a dream framework would in all probability be too hard an ask to deliver on. The field of EBR is perhaps too wide, diverse and complex to capture in a single framework. However, I do think on a certain level of generality, broad parameters for ethical EBR can be articulated, and this is what I propose here.

In my search for the development of an applicable or relevant list of principles, I considered different references, which include but are not limited to the following: the regulatory framework in South Africa, provisions of the national strategy regarding ethics committees, the provisions of international conventions, relevant academic literature and environmental philosophy literature, the concerns of EBRECs, established codes for research ethics integrity and codes of conduct for human and animal research ethics. I also scrutinised the many different ethical frameworks dealing with environmental and biosafety research ethics and biotechnology practices.

In these frameworks, I determined the following principles as crucial and necessary in EBR: precaution, containment, reduction of dual-use harms, care for the environments and all living organisms, sustainability, safety, fairness, respect, replacement, reduction and refinement (the three Rs), avoidance of bias, social responsibility, responsible conduct of research, scientific integrity, respect for biodiversity and cultural diversity, protection of communities and the responsible treatment of cultural heritage.

Bringing this all together in a practical, easily manageable reference set of principles resulted in four categories of principles that I want to recommend. The following section will discuss these categories in more detail.

5.3 Recommended principles for EBRECs in the South African context

The most challenging consideration in compiling a manageable meaningful list of principles for EBRECs in the South African context entails that the complexity and the multidisciplinary area of EBR be acknowledged. This is not an easy task considering the various efforts by different role players and trial actions within specific disciplines. Although EBR is not about and is separate from human ethics, biotechnology still deals with human lives. Therefore complementary ethical codes and principles that consider respect for persons and animals and respect for the natural environment form the foundation of ethical principles in any discipline.

I anticipate, or rather hope, that my proposal and recommendation in this study will be a small step towards a much needed, more uniform national framework for EBRECs in South Africa. A holistic approach to cover the extensive spectrum was the only way to tackle this enormous task. That means to see the big picture and consider the whole or complete system. Thus, it will acknowledge humans, technology and the environment as a single system and principles should, therefore, follow local and international laws, regulations and value sets (MAIEI, 2020).

With that in mind, I propose four categories: Moral, Social, Legal and Safety. For ease of reference and recollection, it can be referred to as **MSLS**. Below I will name the relevant principles in each category, and I will elaborate and explain them as a humble effort to cover the broad EBR spectrum.

The ethical- and decision-making framework of principles that I wish to suggest is based on the idea that there are many ethically relevant dimensions upon which any research can fare better or worse. Rather than drawing a sharp line between ethically acceptable and ethically unacceptable, these recommended categories with their respective directive principles are designed to indicate where a study falls on an ethical spectrum. The ethically good or praiseworthy studies are on the one end of the spectrum, and the unacceptable or ethically

problematic ones on the other end. The aim should be to have research that is as far as possible towards the ethically acceptable side of the spectrum.

5.3.1 Principles as a Moral Concept

Principles as a Moral Concept can be seen as principles that are used to guide our actions; in other words, they are rules of personal conduct. They serve as the foundation of imperatives and foster ethical research practices (Richardson, 2018).

5.3.1.1 Rigour

The principle of Rigour as a moral concept refers to the act of skill and care in scientific work. Rigour can be mentioned in connection with honesty and integrity and to prevent corrupt practices and professional misconduct. An EBREC should encourage strict adherence to the scientific method.

5.3.1.2 Respect

The principle of respect requires in the first instance to value alternative viewpoints and respect the different ethical differences resulting from local customs, laws or cultures. It also speaks to respect for life and the environment. Researchers should justify and minimise any possible adverse effect their work may have on the natural environment, animals and people. It includes respect and adherence to the law and ensuring that research is done lawfully and in a justifiable manner.

5.3.1.3 Responsibility

The principle of responsibility puts the onus on the researcher to ensure environmental protection and biosafety. The researcher thus commits and needs to be accountable for ensuring environmental protection and biosafety during all stages of the research (Indian Council of Medical Research, 2016).

At the same time, the principle of responsibility asks of a researcher to engage in studies that they are qualified to perform. That means choosing appropriate research methods to avoid results of a misleading nature. In all disciplines, professional responsibility and competence is a prerequisite. Professional competence puts a responsibility on researchers to have the necessary knowledge, awareness and training for the task (Weinbaum *et al.,* 2019: 32).

With cross-disciplinary fields, researchers could be challenged to bring the necessary expertise and competence to the team. EBRECs should thus be aware of the challenges in this regard and ensure that the appropriate knowledge and competence are available before a project can be approved.

It is also the responsibility of researchers and the committee to know and understand legislation applicable to research and to comply with such legislation.

5.3.1.4 Replacing unsustainable materials

The principle of replacing requires that researchers replace unsustainable materials to lower the ecological footprint and help to bring about sustainability. The replacing principle respects biodiversity, but the alternative method should not be harmful to the environment. An EBREC can direct researchers to use simulations or natural experiments whenever possible, instead of using live models that can negatively affect biodiversity or the biosphere.

5.3.1.5 Reducing the use of resources

The reducing principle would guide researchers to minimise the impact of research activities on the ecosystem(s).

5.3.1.6 Refining practices to develop a positive environmental balance

The refining principle in EBR will lead researchers to collaborate and streamline research activities to use the least intrusive or disruptive methods available to achieve research objectives.

The three Rs above are similar to the three principles for Animal Ethics but are applied in Environmental Ethics to lower the ecological footprint of research and to connect with the sustainability principle (Crozier & Schulte-Hostedde, 2015: 585).

5.3.2 Principles as a Social Concept

5.3.2.1 Beneficence and Non-maleficence

According to Houde and Dumas, the principles of Beneficence and Non-maleficence are the heart of ethics for all organisms (2007: 8). These principles require that research should provide value that outweighs harm or risk and the research should be worthwhile. Robust precautions should mitigate potential risks. The aim is thus to maximise the benefit while minimising the risk of harm. The EBREC should ensure that discoveries in bioscience and biotechnology research and the generated knowledge, for example, does not facilitate bioterror (Weinbaum *et al.,* 2019: 10).

Beneficence in research is to do good and perform the positive action to contribute to the welfare of the environment or a community. At the same time, non-maleficence is the principle to avoid harmful acts. This requires that researchers should act in a way that is not detrimental to organisms and adhere to be good towards all forms of life (Houde & Dumas, 2007: 8).

5.3.2.2 Non-exploitation

Violation of the non-exploitation principle mainly occurs when research is conducted in countries with less stringent regulations on research, constituting what was identified in Chapter 3 as the problem of ethics-dumping. This principle should especially be monitored by EBRECs when research is conducted in developing countries. Research conducted outside the proximity of an EBRECs legal framework is a matter of particular ethical concern. But exploitation may also occur when researchers use traditional knowledge for their own benefit and restrain the country or community from the benefits of the results. Since researchers in developing countries do not always follow the correct ethical protocols, EBRECs should be aware of the ethical issues in this regard and use this principle to alert researchers of possible or actual violations in this area. Avoiding possible exploitation could be achieved with collaborative partnerships that can also reinforce other ethical principles, such as a duty to society (Weinbaum *et al.,* 2019: 8).

5.3.2.3 Duty to Society

An EBREC should start with the question, what will be the benefit of the research for society? The primary premise of duty to society is that research should benefit the community.

It is essential to understand ethical boundaries, values and concerns regarding the effect of the research on the society or community. The International Society of Ethnobiology explains it as follows: "persons and organisations undertaking research activities shall do throughout in good faith, acting in accordance with, and with due respect for, the cultural norms and dignity of all potentially affected communities, and with a commitment that collecting specimens and information, whether of a zoological, botanical, mineral, cultural nature and compiling data or publishing information thereof, means doing so only in the holistic context, respectful norms and belief systems of the relevant communities" (ISE, 2008: 9-10). Researchers must consider the perspectives of diverse communities to understand their values and ethical boundaries and how the research will affect the community (Weinbaum *et al.,* 2019: 8)

The point being made here is that the acceptability of research should depend on the extent to which it will be acceptable internationally, and should thus involve consultation, coordination, negotiation and active engagement with other countries where necessary (Selgelid, 2016: 925–926).

In disciplines where research rarely includes research participants, e.g. engineering, the duty to society means public safety. In ecology, it means the management of ecosystems, understanding the ecosystems' complexity and biodiversity and minimising species losses. In other words, in disciplines that are non-human centric, this principle means to reduce the harm to the environment (Weinbaum *et al.,* 2019: 9).

Duty to society can also pose an ethical dilemma in disciplines such as information science research conducted on society-wide data sets. The latest POPIA requirements play an important role in delineating the principle of duty to society, also in research. Researchers and EBRECs should thus familiarise themselves with all the ethical aspects of this Protection of Personal Information Act and the consequences for research.

5.3.3 Principles as a Legal Concept

5.3.3.1 Precautionary Principle

The ASTEC definition for the Precautionary Principle is:

> A principle dictating that where there is threat of serious irreversible environmental damage, lack of full scientific certainty should not be used as a reason for postponing measures to prevent environmental degradation. In the application of the PP public and private decisions should be guided by careful evaluation to avoid, wherever practicable, serious or irreversible damage to the environment, and an assessment of the risk-weighed consequences of various options (ASTEC: 1998: 84).

The UN Convention on Biodiversity asserts that biodiversity risk should override scientific uncertainty concerns.

The Precautionary Principle was first articulated in 1987 in the Montreal Protocol; however, Hans Jonas was the first contributor to this principle in 1979, later translated as *The Imperative of Responsibility.* This contribution is the philosophical foundation of the PP and was voiced as an ethical turn (Origgi, 2014: 6). The principle calls explicitly for cases where scientific uncertainty plays a significant role and where harm is anticipated. It can be motivated as a better-safe-than-sorry approach (Weinbaum *et al.,* 2019: 45). However, what is harmful to some is not harmful to others. Others may sometimes even benefit. The favourable option would then be to avoid and minimise risk or to select the least harmful alternative (Hermerén, 2011: 378).

The PP embraces the four Ms (maxims) for activities in environmentally sensitive and protected areas.

- Movement: Rather move away from the protected or sensitive area or use non-invasive techniques;
- Minimisation of procedures but ensure statistical requirements;
- Modification of activities and experiments to reduce the impact on the environment; and
- Maximisation of the benefits and the use of the research results (ASTEC,1998: 75).

With the precautionary principle, intervention by an EBREC can avoid or diminish harm to the environment and biodiversity.

According to the European Commission, the precautionary principle can be extended to the protection of dignity (for example, in communities) and the right to the protection of personal data and therefore should go beyond the scope of physical damage to humans, animals or the environment (UNESCO Report, 2005: 3).

The PP motivates a "better-safe-than-sorry approach" to the decision-making process of an EBREC, thus motivating forbearance (Weinbaum *et al.,* 2019: 45).

Decisions and recommendations need to be proportional to the seriousness of the potential harm, considering positive and negative consequences and assessing the moral implications (UNESCO Report, 2005).

5.3.3.2 Proportionality

The principle of proportionality originated in German case law and must be seen in conjunction with three conditions: appropriateness, necessity and reasonableness. This principle can directly be linked to the precautionary principle and is, in effect, an extension thereof. Proportionality means the action must be a “rational means to a permissible end” (Engle, 2012: 1). Michael Selgelid from Monash University indicates that the acceptability of extraordinarily risky research depends on the extent that there will be a reasonable expectation of ultimate results where the benefits outweigh the risks involved (Selgelid, 2016). As such, this principle can be a helpful guide in the decision-making of EBRECs and EBR. The point of the principle is that the evaluation of serious risks should also satisfy the greater requirement of ethical acceptability. The greater the expected benefit of the research, the more ethically acceptable it would be for the community, funders and publishers.

The European Group on Ethics (EGE) explains the principle as follows:

> The principle of proportionality includes that research methods are necessary to the aims pursued and that no alternative, more acceptable methods are available (Hermerén, 2011: 374).

This can be explained in the following way. If there are more than minimal risks involved and the methods used in the research project are controversial, the intended goal should be important otherwise it will be hard to justify the use of these controversial methods.

If we think back to the examples covered in Chapters 2 and 3, the general goal of research is to obtain new knowledge. Considering the Covid-19 examples and the challenges and development of vaccines, if an EBREC needs to assess the appropriateness of some of these

means, they need to acknowledge possible adverse effects, including biosafety issues or dual uses. Synthesisers, as an example that is more available in many different research fields, and can, for example, be used for biological warfare. Therefore if the ethics reviewers consider the proportionality principle, they need to determine if the same objective can be achieved through a less controversial or dangerous method, and advise the researcher accordingly. However, if the research objective is important, as with Covid-19 research and no other research method is available, it may justify more extreme or dangerous experiments, but only if the conditions of appropriateness, necessity and reasonableness are considered.

Embryonic stem cell research is another example mentioned in Chapters 2 and 3, and an EBREC will also in this context use the proportionality principle to assess if the means of the research are appropriate to the goal.

5.3.3.3 Equity

Inclusiveness in research is essential, and the fair distribution of benefits and burdens should be an important consideration for EBRECs. Issues of fair and equitable treatment are important in including a community in a research project as well as consideration of the basis for the exclusion of others. Equity can thus be understood as social justice or fairness, and it is grounded in distributive justice and value judgements.

5.3.3.4 Environmental Justice

The concept of Environmental Justice emerged in the early 1980s in the United States of America. It refers to the “fair” distribution of environmental benefits and burdens. It also refers to recognising communities and their way of life, their local knowledge and understanding cultural differences. Unjust research practices include practices causing harm to communities or the environment without any compensation and taking advantage of vulnerable situations. (Selgelid, 2016: 13). It will be unjust if the risk or the benefit of the research is only for some people or communities and not for the greater good of all. It all comes down to equal treatment. As with other legal concepts, justice is linked to equity, having equal risks or benefits and ensuring equitable sharing.

The principle of Environmental Justice is embodied in the Rio Declaration and relates to issues of compensation, distribution and liability to achieve environmental protection. Causing environmental damage is ethically reprehensible (IAEA, 2002: 16–17).

5.3.4 Principles as a Safety Concept

Principles as a Safety Concept requires of EBRECs and researchers to ensure environmentally safe applications of biotechnology. It also concerns the safety of biological

materials in the environment and the safety of all biotechnology practices in all possible research areas.

Safety questions should be regarding the nature of the organism(s) involved, the environments where it is to be researched or released, and how it will influence other species. Considering the consequence, for example of GMOs, it is argued that the impact of GMOs on the environment can be threefold: 1) Direct impact refers to biosafety in the narrower sense of the word, and pertains to concerns regarding evolutionary, ecological or biological impact. 2) Indirect impact refers to the consequences of new technology deployment and 3) Secondary impacts refers to socio-economic and sociological concerns in the development of new technology (Krattiger & Lesser, 1994.: 353).

Principles as a Safety Concept is thus a far-reaching concept for committee reviewers and with EBREC assessment. EBRECs should apply the fundamental principles of risk management and risk assessment. Most countries have biosafety regulations in place, but as indicated in Chapter 4, developing countries, including South Africa, do not have adequate monitoring procedures. The onus is thus on EBRECs to ensure adequate safety and biosafety measures in all applicable research actions and areas of EBR and biotechnology.

5.3.4.1 Safety

The Safety Principle will ensure that researchers follow policies and procedures to ensure the environmentally safe application of biotechnology materials and practices.

It is a containment principle to prevent the unintentional exposure of biological material and it also prevents accidental release of hazardous organisms. The previous chapters indicate that this includes many types of biological material, such as plant, animal and human pathogens, proteins and nucleic acids, including samples and other by-products. Thus, it concerns biological material and the safety thereof in the environment, the direct biological consequences of research practices and the implication for the environment. The Safety Principle will thus cover questions such as the nature of the organisms to be released or the environments where they will be released and what species interaction will entail (Krattiger & Lessser, 1994: 356). According to the National Academy of Science in the USA, "safety assessment should be based on the nature of the organism and the environment into which it will be introduced, not on the method by which it was modified" (Krattiger & Lesser, 1994: 360).

The principle also covers the protection of researchers and research participants, research environments and the public and communities against hazardous biological agents. It also covers the protection of animals and plants and the protection of the environment. EBRECs

can apply the safety principle by assessing the risks, by estimating the risk factors in terms of the likelihood of hazard occurrence and the possible severity and consequences. A further step will be to minimise the risk level, either by recommending better management strategies or to stop a given activity if the risks are unacceptable (Collard *et al.,* 2009: 3-4).

With the Safety Principle, the risk assessment should consider the characteristics of the involved organisms and newly introduced traits, and the intended use of the micro-organisms. This requires consideration of how such micro-organisms are to be contained by biological, chemical or physical barriers or the impact if released into the environment. Additionally, the assessment should also investigate the area and characteristics and the interaction where the activity or the biotechnological process will take place.

The regulatory requirements regarding biosafety practices, nationally and internationally, should importantly thus also be known and accessible to researchers and EBRECs.

5.3.4.2 Security

The security principle refers to biosecurity and research or technologies with the potential to be misused. The security principle measures protection against intentional misuse, theft or release of biological material for the wrong reasons. The principle ensures responsible conduct and reasonable oversight of EBR and the prevention of the development of biological weapons for bioterrorism.

EBRECs should thus also be knowledgeable about national and international regulatory frameworks with provisions on the handling of biological materials.

5.3.4.3 Sustainability

The principle of sustainability means researchers need to refrain from overexploiting natural resources and limit environmental damage. Applying the principle of sustainability, the EBREC should reduce chemical inputs and harmful research practices. Sustainability can be seen as a relationship between society and the environment but according to Nelson and Vucetich (2012), the relationship is affected by our technologies. The relationship involves the physical aspect, which is the exploitation and an ethical attitude. They explain it by indicating that sustainability involves five dimensions: 1) Develop efficient technologies to meet human needs – the purview of biotechnology, physical science, engineering and economics, 2) Understand ecosystems – the purview of environmental science and ecology, 3) Understand how ecosystems are affected by exploitation – the purview of applied environmental science and applied ecology, 4) Understand how human cultures are affected by exploitation – the purview of anthropology, sociology, policy, law and political science, 5) Understand normative concepts and their meaning, concepts such as depriving human needs, ecosystem health and

social justification – the purview of ethics and philosophy (Nelson & Vucetich, 2012). Ethical attitudes are thus a critical aspect of sustainability.

Interpreting the scope of the Principle of Sustainability, a number of considerations will have to be taken into account by the EBREC, one of them is an understanding that environmental sustainability is important for economic growth and social justice and impacts future generations (IAEA, 2002: 14). Another consideration already formulated in the Rio Declaration is that an acknowledgement of the traditional practices of indigenous people is also highly important in the achievement of sustainability.

5.4 Suggestions for implementation

Part of the proposal of this thesis is that I foresee the implementation of the principles listed above to take place in three phases: 1) Planning, 2) Implementation and 3) Post-approval monitoring.

During the planning phase, EBREC members will receive well-planned training. First it will entail training to explain the principles, the application thereof and the implementation. This will be followed up with practical training sessions. An important step will be to clarify the differences in applying these proposed ethical principles compared to the well-established human and animal ethics principles. I have indicated in Chapter 4 that principlism combined with casuistry (which entails a case by case judgement) could be a valuable tool for ethical decision-making in EBR. In my view principlism will always be the primary method in decision-making in EBRECs, but casuistry is necessary to assist in complicated ethical decisions as an additional supporting tool. The assessment tool will thus be different from other well-known research ethics practices.

With the second, implementation phase, committee members will have the opportunity to test their skills acquired in the first phase and to test whether these skills work. In this phase the EBREC will have to implement opportunities and processes of self-assessment and reflection in order to learn from mistakes in a manner that is not detrimental to the research or the review process, or to identify gaps in knowledge, insight or procedures that need to be addressed.

The post-approval monitoring phase should include good communication between researchers and the EBREC concerning the applications of biotechnology and its related elements. In this regard it is of course not the intention to prescribe a formula for EBRECs to operationalise. Still, instead, EBREC members and researchers, all of whom are academics from different disciplines, will rather be invited to participate in a dialogue and exchange experience with the aim of working towards a mutual interpretation and understanding of the

meaning, implications and requirements for the implementation of the ethical principles of EBR that I propose here.

What I am driving at in this regard, is that this set of ethical principles for EBRECs in the South African context can only set the broad parameters for concrete ethical evaluation, but their actual implementation is still open to different interpretations that will require an ongoing and self-conscious conversation to narrow down its meaning in particular research contexts. I acknowledge that to participate in this conversation will require a certain measure of education and training for all stakeholders involved and for some, even a new kind of education and training. It also will require flexibility and adaptability and the willingness and aptitude to participate in multidisciplinary working groups and conversations. Daunting as this kind of collaboration seems at first glance, it seems to be necessary in light of the far-reaching advances in the research that falls within the ambit of EBRECs.

Collaboration on another level also seems to be a prerequisite for the successful implementation of the principles that I have identified above for responsible and ethical practices in EBR, and this entail collaboration between different research ethics committees. The different ethics committees should interact with each other in the first place regarding the scope that the various committees handle. The Human Ethics Committee needs to be involved where human participation and consent is applied, while the Animal Ethics Committee will cover concerns where sentient animals are involved. In a similar vein, the Health Ethics Committee should become involved when EBR and the terrain of human health overlap. In my view, such interaction between the different sciences and ethics committees, such as the Health, Human and Animal Ethics committees, is necessary, but there is an even more fundamental level on which collaboration between them should be sought. In some instances, it will be required to obtain ethical approval from more than one of the ethics committees, given the current institutionalisation of ethics committees on the one hand and the blurring of boundaries between disciplines and research fields on the other hand. This level of collaboration, however, seems to me to raise more than just questions about the scope of each committee and its jurisdiction, it rather starts to raise questions about the need for the merging of committees in certain cases and figuring out how to converse with one another about concerns and responses that go far beyond conventional disciplinary boundaries.

5.5 Themes for further research

I hope that this study will generate discussion in further refining the principles and the implementation thereof by all EBRECs in South Africa. An important theme for further investigation should be to fill the gap between the research findings of this thesis and the practical implementation in a South African context.

Additionally, another question that is still vague is the responsibility of an EBREC concerning international law and international codes of conduct. It can be said that EBRECs are the first in line in the national and international system for safe biotechnology research to safeguard our planet, humans, animals and the environment. But the question remains what the boundaries for consideration of an EBREC are. Where does the responsibility of the ethics committee start, and where does it end? Can EBRECs be held responsible in cases of serious adverse events? What should be done in cases where EBRECs have done all the work that could reasonably be expected of them, but they were misled by a researcher or a research team? Should EBRECs assume the role of a mentor regarding researchers reporting to it? But how far should this mentorship be taken and from where should researchers themselves take responsibility. And what should be done if things go wrong after such mentorship? Who takes ultimate responsibility?

Furthermore: EBRECs already fulfil an enormous task, organising training programmes, checking researchers' experience and expertise in the research field, monitoring research work and forcing the researcher to comply with all the relevant biosafety rules and ethical principles. EBRECs also need to check all the legal aspects, e.g. export and import of GMO material and stop research that does not follow biosafety measures, but do they make a difference in the unethical conduct of research on a local and an international level? While other ethics committees are focused on either humans or animals or health, the remit of EBRECs is much broader and complicated, taking into account dilemmas that new technologies raise for societies as a whole. Further investigation of these critical questions will be of great value for EBR and biotechnology practices.

Another avenue for future research is the questions raised by the recently implemented Protection of Personal Information Act (POPIA) and the European General Data Protection Regulation (GDPR) insofar as they are related to research vetted by EBRECs.

Lastly, a productive avenue of research could perhaps be found in an investigation of the implications that the blurring of disciplinary boundaries caused by recent advances in science and technology may have for ethics committees in general and EBRECs in particular. As the very nature of technology and innovation are being re-interpreted, including our relationship to the natural and the ecological, and as the parameters of safety and security seem to be shifting as we speak, it may require of us to also rethink the nature of our ethics, our knowledge, our disciplinary boundaries and how we assess research proposals and grant them permission to go ahead.

While we are still a long way removed from such an investigation, I hope that this study has at least started to open our thinking in this direction.

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APPENDIX A: SEARCH RESULTS

The search results in six major electronic databases indicate the lack of relevant literature on the research topic.

I decided not to use a systematic review approach, but rather a scoping review method, as this is a relatively new approach to evidence synthesis (Munn, 2018: 1). Munn indicates that a scoping review is a useful tool to "determine the scope or coverage of a body of literature on a given topic and give a clear indication of the volume of literature and studies available as well as an overview of its focus" (2018:2). He also suggests using a scoping review for the following purpose, “to identify types of available evidence in a particular field, to clarify concepts/definitions in the literature and to identify and analyse knowledge gaps" (2018: 2).

Using this method requires an investigation into a comprehensive set of databases and websites to identify relevant resources. The scoping review can more easily reveal the research gaps and the lack of investigated and reported knowledge in a specific field.

The scoping review method also offers baseline data regarding the availability of research on the topic. The results are presented via graphs to explain the outcome more easily because results may be difficult to read and interpret. With this method, applicable data on the topics can be explored and summarised (Lockwood, 2019: 291).

Search descriptors for EBSCOhost Web were filtered to include ten databases on this platform. These included Academic Search Ultimate, Africa-Wide Information, Applied Science & Technology, CAB Abstracts, Green File, Kovsiecat, KovsieScholar, MasterFile Premier, Open Dissertations and Philosophers Index with Full Text. The search in EBSCOhost was limited to Full Text and Scholarly (Peer Reviewed) Journals.

Sifting through the indicated results shows that very few were relevant to the research topic. Example: A search in EBSCOhost with the following keywords *“Environmental and Biosafety Research Ethics”* produced 2 340 results, but with the following message: "**Note: Your initial search query did not yield any results.** However, using SmartText Searching, results were found based on your keywords." (EBSCOhost search results). The results, in the example, were mostly unrelated.

ELECTRONIC DATABASE SEARCHES RESULTS

The relevant keywords are highlighted in blue.

Keywords 1970–2020	EBSCOhost Filter 10 applicable databases	NRFCurrent and completed research SABINET	Science Direct	Web of Science Filter open access	Glob-ethics net	Academic Search Ultimate (Multidisciplinary database)
Research Ethics	26 417	1 727	448 536	12 800	6 830	16 533
Environmental Research Ethics	88	81	84 179	478	1 280	35
Biosafety Research Ethics	4	0	1 948	7	1	2
Environmental and Biosafety Research Ethics	1 340	0	658	1	1	2 870
Human Research Ethics	2 546	345	265 021	2 492	2 220	1 859
Animal Research Ethics	360	32	137 700	373	684	178
Research Ethics Principles	278	247	66 240	1 088	1 340	172
Environmental Research	4	12	18 866	146	826	2

Ethics Principles						
Research Ethics Committee	5 558	34	340 031	3 474	683	3 724
Keywords *Advanced Including* ***AND***	**EBSCOhost**	**Google Scholar**	**Science Direct**	**Web of Science**	**Glob ethics net**	**Academic Search Ultimate (Multidisciplinary database)**
Environmental and Biosafety Research AND Ethics Committee	2 (not related)	0	509	0 – No records found	1	1
Human Research ***AND*** Ethics Committee	1 315	8	204 180	947	513	626
Animal Research ***AND*** Ethics Committee	278	0	114 738	104	184	66
Human Research ***AND*** Research Ethics Principles	146	80	46 129	835	839	51

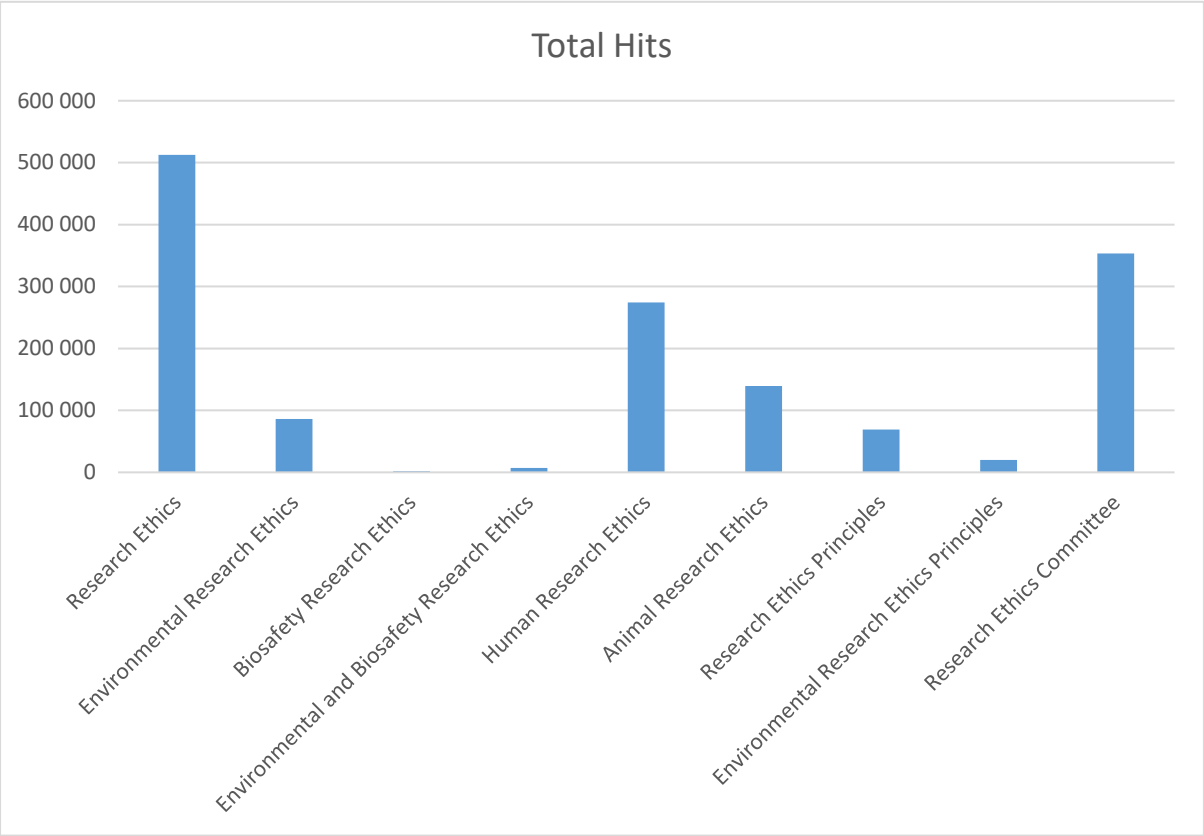
Animal Research ***AND*** Research Ethics Principles	22	8	19 311	145	281	1
Environmental and Biosafety Research AND Research Ethics Principles	0 No results	0	280	0 – No records found	1	0
Research Ethics Principles ***AND*** Humans ***AND*** Ethics Committee	187	1	28 642	85	745	10
Research Ethics Principles ***AND*** Animals ***AND*** Ethics Committee	48	0	13 638	39	310	371
Research Ethics Principles AND Environmental and	0 – No results	0	213	0 – No Records	1	0

Biosafety AND Ethics Committee						

The total hits in all the database searches per keyword are indicated in the graphs below. The relevant keywords for this study are highlighted in blue:

Basic keyword search:

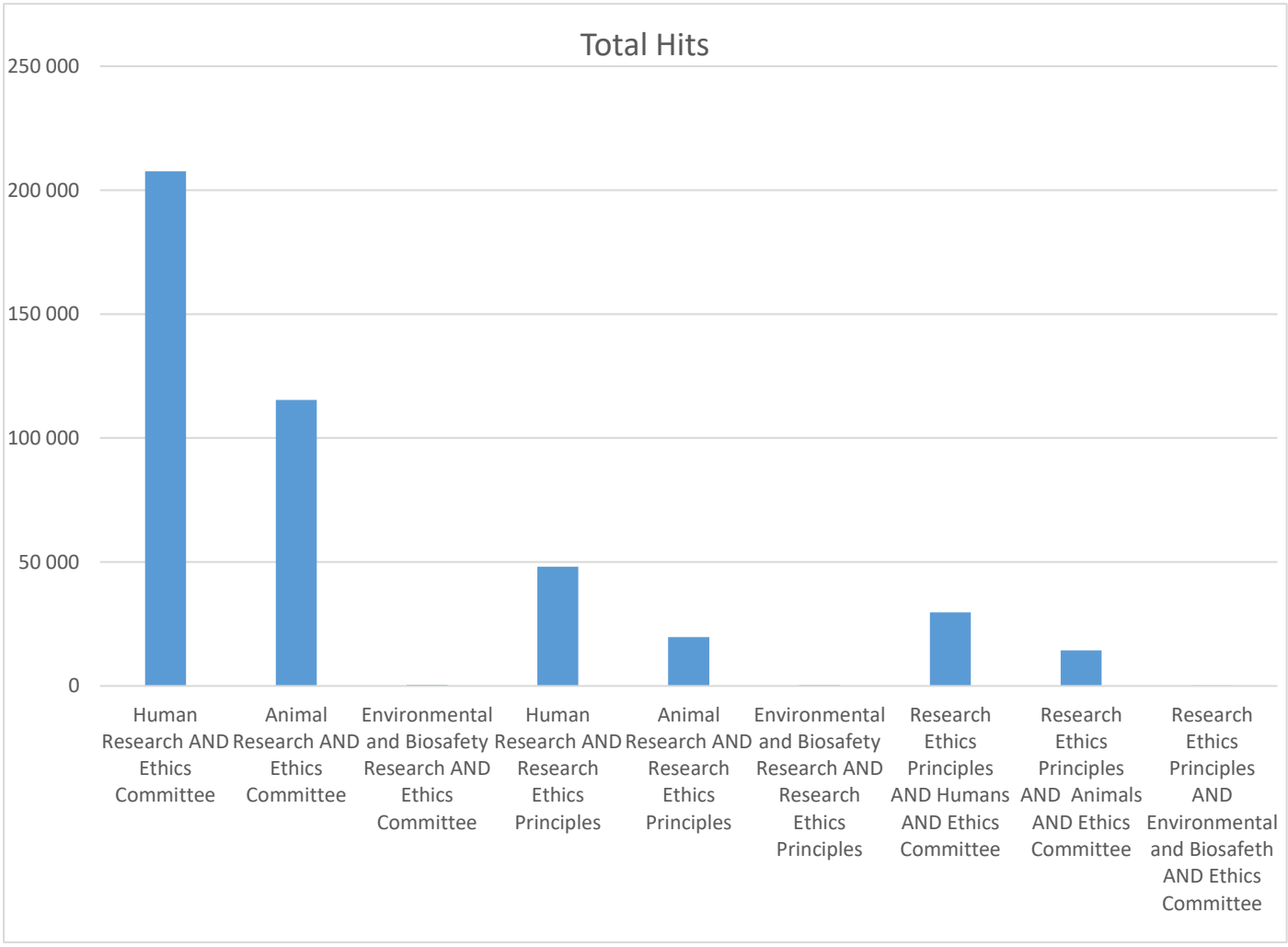
KEYWORDS	TOTAL HITS
Research Ethics	512 843
Environmental Research Ethics	86 141
Biosafety Research Ethics	1 962
Environmental and Biosafety Research Ethics	6 868
Human Research Ethics	274 483
Animal Research Ethics	139 327
Research Ethics Principles	69 365
Environmental Research Ethics Principles	19 856
Research Ethics Committee	353 504



Advanced Keyword search including AND:

KEYWORDS	TOTAL HITS
Human Research ***AND*** Ethics Committee	207 589
Animal Research ***AND*** Ethics Committee	115 370
Environmental and Biosafety Research ***AND*** Ethics Committee	513

Human Research ***AND*** Research Ethics Principles	48 080
Animal Research ***AND*** Research Ethics Principles	19 768
Environmental and Biosafety Research ***AND*** Research Ethics Principles	281
Research Ethics Principles ***AND*** Humans ***AND*** Ethics Committee	29 670
Research Ethics Principles ***AND*** Animals ***AND*** Ethics Committee	14 406
Research Ethics Principles ***AND*** Environmental and Biosafety ***AND*** Ethics Committee	214



The graph results give a good indication of the lack of literature in the mentioned fields.

The uncertainty and complexity of research in this broad field of study makes decision-making and the formulation of guiding principles challenging. Crozier and Schulte-Hostedde (2015:580) recognise that there are relatively few publications on environmental research ethics (ecological research and field studies) available. While extensive works of literature are available on environmental ethics in general, literature on conservation ethics and animal research ethics is scarce. Several papers indicate the ethical challenges and concerns in environmental research ethics and made some recommendations, but no proof of any measurable solutions or progress could be found.

APPENDIX B: INTERNATIONAL FRAMEWORKS AND UNIVERSAL CODES

1. The Nuremberg Code (1947)

https://ivrit.co.za/Maricel/The_Nuremberg_Code%201947.pdf

2. The Declaration of Helsinki (1964)

https://ivrit.co.za/Maricel/Declaration%20of%20Helsinki.pdf

3. The Belmont Report (1979)

https://ivrit.co.za/Maricel/Belmont_Report_1979.pdf

4. CIOMS – International Ethical Guidelines for Biomedical Research Involving Human Subjects (1991)

https://ivrit.co.za/Maricel/WEB-CIOMS-EthicalGuidelines.pdf

https://ivrit.co.za/Maricel/International_Ethical_Guidelines_for_Biomedical_Research_Involving_Human_Subjects.pdf

5. Universal Code for Scientists (2007)

https://ivrit.co.za/Maricel/universal-ethical-code-scientists.pdf

6. The Singapore Statement (2010)

https://ivrit.co.za/Maricel/singapore_statement_EN.pdf

APPENDIX C: ADDITIONAL EXAMPLES OF BIOTECHNOLOGY

In chapter two, the scene was set with various examples within the colour groups as per Dr Rita Colwell's biotechnology categories. Only a few examples to highlight the ethical concerns regarding EBR in action were discussed. Many fascinating examples were discovered in my literature research, which I decided to share here for completeness and for the sake of interest. In the thesis, examples from red, green, white, grey and orange biotechnology were shared.

I, therefore, want to share some other examples from yellow, blue, gold, brown, black and violet biotechnology research activities.

Yellow biotechnology: This refers to Food Biotechnology that mainly focuses on food production and nutrition science. For example, it includes research to reduce the levels of saturated fats in cooking oils. It has gene modification, vitro cell culture technology and biological infection control. Yellow biotechnology is an emerging research field that can also be explained as biotechnology with insects, bio-engineered to make better food. Active genes in insects are used for medicine and agriculture applications. Insects can survive in extreme habitats due to diverse biological and chemicals systems, and the core components of these systems are enzymes such as amylase, lipases and peptidases.

Food production – using insect enzymes for cultured meat

Cellular agriculture technology products typically obtained from livestock farming are manufactured using culturing techniques that required no or significantly reduced animal involvement. Examples are cultured meat, egg white, milk and leather (Steiner, 2020: 40). The correct term for cultured meat is "artificial muscle proteins" because *meat* implies animal slaughtering, which is not the case with cultured meat (Stephens *et al.,* 2018: 157). It is well-known that the meat industry has a pervasive effect on global environments, leading to 24% of greenhouse gas emissions (ibid).

Professor Mark Post from the Maastricht University produced the world's first cultured beef burger in 2013 (Stephens *et al.,* 2018: 156). Compared to conventionally produced meat, studies show cultured meat creates 78–96% less greenhouse gas emissions, 99% less land use, 82–96% less water use and approximately 45% less energy use (ibid: 157). Cultured meat could be life-changing technology addressing environmental and food security issues. (ibid: 164). Cell cultures or genetically engineered microbes could also assist in reducing or eliminating the suffering of farmed animals but the ethical evaluation of this kind of scenario remains difficult (Mohorčich & Reese, 2019: 1).

Academic literature on ethics generally reports supportive arguments for cultured meat, but certain ethical concerns and consumer acceptance needs consideration. Consumer resistance may be due to prior belief structures; for example, insects or products from insects for food purposes are strange and controversial for Western countries. EBRECs need to consider the cultural beliefs of the consumer and ensure proper testing of the product to guarantee safety and reliability. Respecting cultural traditions is an important ethical consideration.

Another ethical problem can be economic risk and affordability for poor communities. The higher the cost of the research, the higher the perceived financial risk. The research cost of Professor Post's first beef burger was over $311 000 (Niglia, n.d.: 1). The economic viability should therefore be an ethical consideration.

Biosafety measures should also be in place to identify possible dangerous pathogens and to avoid contamination. Physical risk is always an ethical concern; therefore, the reluctance of consumers to accept new cultured products.

A possible safety issue is potential food fraud through adulteration of food to gain financial benefit (Stephens *et al.,* 2018: 163). Shears (2010) as well as Spink and Moyer (2011) mentioned that deliberate adulteration of food becomes an issue worldwide. EBRECs need to be alert regarding non-compliance issues, namely 1) violation of laws, 2) intention, 3) economic gain, and 4) customer deception (Kowalska, 2018: 1277). An EBREC is in the position to prevent, control and mitigate possible food fraud to protect the consumers.

The effect of the research on conventional agricultural practices also needs ethical attention. There is also a reluctance to accept fertilisers, insecticides or herbicides for fear of soil damage or health-related issues. It is the task of an EBREC to weigh the benefits against the possible harm.

Related social, political and institutional implications may cause ethical issues. The following questions can be asked: Does the benefits increase the consumer's risk and possibly negatively influence the environment? Or is it ethical to sacrifice a tropical rainforest for the production of soya and palm oil products? What is more critical, environmental sustainability or mass food production? (Early, 2019: 45). The task of an ethics committee remains a balancing act between what is wrong and what is right.

Blue biotechnology: This technology is called Marine Biotechnology and is related to seas, oceans, marine resources and aquatic environments to control harmful waterborne organisms or for the use of biofuels obtained from microalgae and other sea resources.

Marine research is quite expensive and poorly developed in South Africa. The Chemistry Department at Rhodes University investigated the bioactive natural products produced by more than 500 marine invertebrate organisms randomly collected from the south-eastern coast of South Africa. The research explored the pharmaceutical potential of small molecules produced by indigenous marine organisms such as sponges and sea squirts and their associated microbes. These molecules, known as secondary metabolites, often have potent biological activity that can be harnessed to develop new anti-cancer, anti-malaria, anti-TB and anti-viral drugs (Bolton *et al.,* 2013: 455–456).

Utilising marine biotechnology faces not only ethical issues but also legal issues. Marine biotechnologists must be careful and conscious to ensure that the ecosystems and species remain stable. Modifying living sea organisms poses possible threats and damages wildlife and habitats, which is an ethical concern. Invasive species such as toxic algae or modified plant species disrupt the ecological balance. Considering the ethical implications, it is evident that an EBREC needs to be equipped with the necessary tools to deal with these ethical questions and scenarios. Regulatory frameworks for the possible exploitation of GMOs are required, but they must be based on reliable, objective criteria.

Insomniac Algae for biofuel compounds

Professor Carl Johnson, a biological scientist at Vanderbilt University, claims that research has shown that manipulating the clock genes of blue-green algae (cyanobacteria) can increase commercially valuable biomolecules. This research promises significant benefits in many ways. Microalgae have various applications such as anti-cancer drugs, cosmetics, biofuels and bioplastics, and it holds substantial economic benefits (Vanderbilt University). However, the main concern that defines the current state of algae biotechnology is the cost. It is an expensive product and microalgae cultivation is challenging because it needs a suitable nutrition medium. According to Ivanina Vasileva and others from Bulgaria, the ethical dilemma with algae biotechnology is between quality and quantity and the ethical decision of producing large quantities of algae to feed the hungry or instead if the quality is selected, the researcher needs to give up on the idea of solving poverty but instead pursue other opportunities in the cosmetic or medicine field (Vasileva *et al.,* 2018: 3).

Algae genes are also transferred into rapeseed and soya, leading to increased omega-3 acids, essential fatty acids vital for normal metabolism. Other exciting research activities include developing proteins from seabed marine life that can be utilised for antifreeze products for

food (Mayer, 2005: 254). Furthermore, applications include wound dressings coated with Chitosan, a sugar typically derived from shrimp and crab shells (Steiner, 2020: 14).

Similarly, other groundbreaking research involves replacing products traditionally sourced from animals that can now be created from algae to produce various products such as vegan milk and cheese. A research project conducted by a PhD student from the University of New South Wales in Sydney describes the marine ecosystem as a diverse resource to obtain food ingredients and enzymes for cheese making and other applications. The “cheddar” cheese was made from a red seaweed available abundantly in the ocean. The product is biologically the same as the animal version but marked as cruelty-free products (Arbita, 2020). A novel idea and groundbreaking technology, but unfortunately not without ethical concerns. It can be acknowledged as bioprospecting, where the biodiversity of the sea is used for commercial purposes.

The ethical, political, social- and cultural challenges and legal aspects of studying and collecting organisms and marine resources are vital, especially when collecting in other countries' territories. This action may lead to biopiracy, which is unfortunate when academic institutions or companies collect unauthorised and uncompensated samples. EBRECs should be equipped to support sustainable development and global conservation of biodiversity, with the necessary knowledge and guiding tools to assist researchers in ethical bioprospecting.

Research and the use of resources and organisms found in the territories of other countries can create various problems and disputes. Richer resources and better selection of marine life does not mean a researcher can proceed without the necessary permission and permits. US scientists are regularly in conflict with the countries south of the equator with their rich marine resources. The complexity regarding property rights under marine governance needs careful ethical consideration and knowledge, including the status of resources in areas beyond national jurisdiction (Collins *et al.,* 2016: 67). Ethics committees should also determine what kind of benefit-sharing will be applicable during such a research project with consideration of the Nagoya Protocol.

EBRECs are also challenged to be knowledgeable in many specialist areas, such as international law. They, therefore, need guiding documentation and well-formulated principles to assist researchers with these complicated ethical scenarios.

Reginal Harrell from the University of Maryland expresses the concern that ethical considerations in marine biotechnology and aquaculture disciplines are limited from a bioethical perspective. Harrel points out that there is a lack of scholarly works regarding the ethics of marine biotechnology (Harrell, 2017: 2). He indicates that bioethical principles are primarily applied to human health and well-being and does not translate to non-human applications (ibid, 2017: 3). Harrell, therefore, questioned the validity of using human bioethical principles, such as autonomy, beneficence, nonmaleficence, justice and respect for marine biotechnology individuals (ibid, 2017: 1). He argues that although research or biotechnology studies are not human-related, it is evident that the benefits of the technology are in principle geared towards the improvement of humans or human activities.

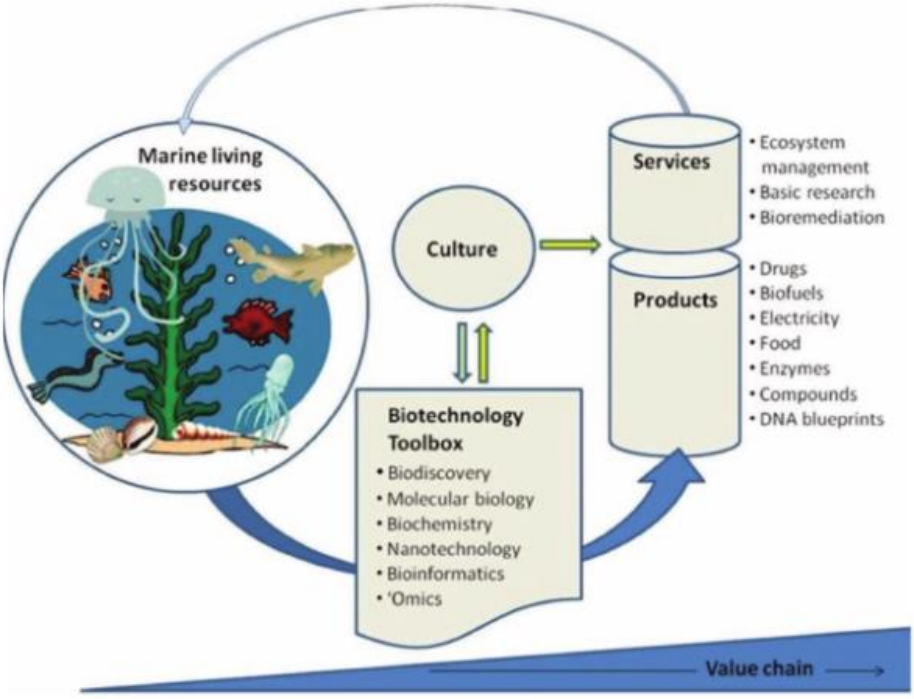


Figure 5: Marine Biotechnology Value Chain (Source: OECD, 2013).

Gold biotechnology is the technology used for everything related to bioinformatics, hardware and software for data analysis of biological processes. It is responsible for obtaining, storing, analysing and separating biological information, e.g. sequencing of peptides, DNA alterations and amino acid sequences, nanotechnology and forensic investigation of crime.

Ancient DNA (aDNA) research

Prof Alan Morris from UCT explains the exciting research with ancient DNA to reveal the secrets of people's movement around Africa. Results recently published included info about

human skeletons from the Mota Cave in Ethiopia, Saldanha Bay in SA, Ballito Bay in SA and Malawi. The article announces the successful extraction of mitochondrial DNA sequence from skeletons that are more than 2000 years old. The research focused on ancient nuclear autosomal DNA to clarify historical past events (Morris, 2017). aDNA research reshaped our view on indigenous populations' demographic histories and gave an exciting insight into ancient history. However, this genomic research holds some ethical implications for individuals and communities. Researchers face many ethical challenges in this complex terrain of aDNA research.

Harm to the indigenous communities can happen due to a lack of consultation and community engagement. Indigenous people believe in the sacred nature of their ancestors and consider this kind of research as "a form of colonialist violence against indigenous people" (Cortez, 2021: 2). Therefore, it is a challenge for the ethics committee to consider this in the review process. Ethical aDNA research should begin with a consultation that includes honesty, transparency and acceptance that some research is off boundaries (ibid, 2021: 14). Another ethical concern is the use of culturally insensitive descriptions and the impact on marginalised groups. Tribal consultation and ethical engagement with communities are essential before any studies using ancient indigenous DNA start. An EBREC should ask if African scientists and descendant communities will be part of the research and what kind of info will be shared regarding their ancestors? In building a knowledge base of our African heritage, the question is how this can be achieved ethically? (Morris, 2017).

The challenge for the ethics committee is to ensure that researchers understand the importance of consultation and collaboration not only before they undertake the research but also during analysis (Cortez, 2021: 13). This kind of research is an excellent example of how more than one ethics committee can be involved in one study. The human ethics committee, as well as the EBREC, need to do an ethical assessment. The human ethics committee will look at the human aspect of the study, while the task of an EBREC will be to concentrate on ethical issues regarding lab work and the destruction of bones in the field of paleogenomics (the study of ancient genomes).

According to Prof Morris, another concerning ethical issue with this kind of research is the destruction of human bone and valuable or rare specimens (Morris, 2017). It means ancient specimens are ground into bone dust in an attempt to get some insight into the prehistory of humans (Callaway, 2018). Human remains can be a valuable source of information, but extracting the best-quality DNA requires the destruction of the bones. The consequences of paleogenomics research raise ethical questions such as: “Does destruction justify the possibility of a new discovery?" Human remains in museums are not only from archaeological

excavations but also from private donors. The lack of ethical guidelines caused a “bone-rush” frenzy among researchers hunting in museums for specimens with the hope of unlocking a great discovery. The ethical implication of the mentioned actions needs careful consideration. According to Handt *et al.* (1994), when specimens in museum collections or archaeological sites are studied, it presents a unique problem in molecular archaeology: the difficulty of verifying and reproducing results through repetition, including the power struggle among the few aDNA laboratories.

In addition Prof Morris argues that the “mining of bone specimens” is inferior science if the only concern for laboratories or museums is because it is ancient and available. He also claims that once the ancient remains are ground into dust, understanding our past and the many hidden stories can be lost forever. It, therefore, challenges the EBREC to recommend less invasive methodologies. This kind of research is probably publication driven in high-impact journals because it can contribute to funding or promotions. How can an EBREC prevent this unethical conduct?

Legal structures and ethical guidelines are not readily available to help researchers determine the best ethical practices in paleogenomics (Bardill *et al.,* 2018: 385). Legislation, such as the National Heritage Resources Act (Act No. 25 of 1999), regarding the protection of archaeological material and the prevention of disturbance or intervention, promotes record-keeping of excavation and collection of archaeological material. The EBREC should be familiar with applicable laws and regulations to ensure scientific standards, and they must also be knowledgeable regarding the required permits from relevant heritage authorities (SAHRA, n.d.: 1).

The ethical question to consider is to determine what is more important: 1) the importance of safeguarding our cultural heritage and treasures against destruction or 2) gaining better knowledge and understanding of the history of humankind. Does the destruction of bones justify the aim to get a better insight into our past?

Furthermore, Prof Morris questioned if ancient DNA can give an accurate picture of the past? Because it could be in terms of lineage but not in terms of adaptation and experience. He explained that reliable sampling should be from the complete skeleton to enable the researcher to compare the genetic and osteological data. He uses the “Denisovans”[57] as an

57 “Researchers were able to piece together a rough composite of a young girl who lived at Denisova Cave in Siberia in Russia 75 000 years ago. The results suggest a broad-faced species that would have looked distinct from both humans and Neanderthals.
Liran Carmel and David Gokhman, geneticists at the Hebrew University of Jerusalem, and their colleagues used only the pinkie of the girl from Denisova Cave to make these conclusions (Price, 2019).

example to strengthen his argument. All the results in the Denisova case were based on three teeth and one finger bone from one excavation site. This case raises an ethical question regarding the scientific integrity of such a small sample.

Furthermore, bones are sent out of the country with parachute research due to the lack of reliable labs in South Africa. Accordingly, another big concern he raised is that different heritage laboratories could get different results from the same sample of ancient bones. The processing methods are not always interchangeable, and the results from different labs are not comparable (Morris, 2017).

Aerial imagery

Exciting research in geology is developing geological information extraction techniques from aerial imagery to explore mining and groundwater or geospatial technologies. Geospatial technologies use analytic methods to analyse a problem or an impact. According to the Penn State College of Earth and Mineral Sciences, it is done through the following steps: 1) define the environment; 2) describe influences of the environment; 3) assess threats and hazards and 4) develop analytic conclusions (Penn State College).

Geospatial technology in research is used to acquire, visualise, store or manipulate geographical information. This method's value enables researchers to collect real-time data from places hard to reach, e.g. dense forests or dangerous environmental disaster zones (Berman *et al.,* 2018: 6). This kind of information assists in disaster management or identifying potential environmental impacts.

Stellenbosch University is a leader in geospatial science research or geographical information science (GIS). Most research relates to data and techniques for environmental and agricultural monitoring. It is also employed for ecosystem service monitoring and wildfire mapping and predictions, biodiversity mapping and climate studies (Van Niekerk, 2020: 316–317).

The ethical dilemmas associated with this kind of research are mostly security concerns or privacy issues, or potential stigmatisation related to a location (Berman *et al.,* 2018: 6). Security, privacy and trust are all intertwined with ethics and law. The violation of privacy constitutes risk and a threat to security. Law provides the resolution, but ethics need to provide the context to the law. With the implementation of POPIA in South Africa on 1 July 2021, all ethics committees need to be aware of the implications. Trust can be disturbed by privacy breaches and is a violation of ethically sound practices. Diverse cultures put different values on privacy, and it needs careful consideration by ethics committees because privacy has an intrinsic social value (Wanbil, 2016: 1).

In a technology-driven information-intensive environment, information security can be complicated due to the risks involved and therefore needs proper information security management, making it an ethical concern. The use of any research technologies and the resulting data, needs critical ethical assessment before implementation.

Brown biotechnology: This kind of technology concentrates on the desert and arid soils. It is also called Desert or Arid Zone Biotechnology. One of the aims is to develop disease-free high-quality enhanced seeds for arid soil and extreme environmental conditions. Brown biotechnology is an important research field as droughts are increasing due to climate change.

Grain engineering

Researchers from the University of Cape Town are working to engineer grain genetically to "bounce back from water deprivation" (Steiner, 2020: 50). The research entails that genes are pulled from a non-edible native plant *(Myroflammus flabellifolius)* with the ability to enter dormancy during drought but bounce back to life in the event of rain.

Similarly, at the Oakridge National Laboratory in Tennessee, researchers attempt more ambitious research to understand how naturally drought-resistant plants use photosynthesis of another nature to endure extreme drought conditions. The goal is to map the agave plant's genetic method of photosynthesis, which is different from other plants. If successful, the genes can hopefully be introduced to all common crops (Steiner, 2020: 51).

With research on genetically modified crops and plants, Albert Weale discussed the following social and ethical issues: Potential harm to human health, the possibility of damage to the environment, the “unnaturalness” of the process and the impact on traditional farming practices due to excessive corporate dominance (Weale, 2010: 582). The ethical question can be asked how sustainable is this kind of research, thinking of the ethical issue of naturalness. An EBREC should first ask what natural is or what can be labelled natural and then secondly ask what is nature and how should we relate to nature? (Asveld *et al.,* 2019: 128). Suppose it is presumed that natural primarily refers to something already existing in nature or produced by nature. In that case, the argument can be that genetically altered processes or products may be acknowledged as natural in certain circumstances. However, different worldviews or differences in beliefs, values or convictions are always an ethical consideration. For some, nature can be seen as fragile that should be handled with care, and the vulnerable ecological balances should not be upset. The perspective that nature is vulnerable envision living organisms as inherently unpredictable, and therefore they believe that it should not be interfered with (Asveld *et al.,* 2019: 129). For researchers, on the contrary, nature is an

essential resource that can solve problems and provide many viable solutions. In research ethics, these two positions need substantial consideration.

These different perspectives also give rise to varying approaches to risk management. The one group sees the risks as undeniable and considerable. In contrast, the other group does not agree and argues that escaping is low and will not significantly impact the environment. An EBREC needs to seek the golden mean considering all risk factors and ethical considerations.

Albert Weale explains the moral imperative: "Modern biotechnologies have a powerful social, economic and political impact locally, nationally and internationally. They need to be evaluated according to the ethical criteria that must always guide human activities and relations in the social, economic and political spheres" (Weale, 2010: 583).

Black biotechnology: This dark biotechnology is all about biological wars and biocriminolgy. It investigates pathogenic, virulent and resistant microorganisms for converting into biological weapons or counteracting their harmful effects. An example is the bacteria *Bacillus anthracis* or *Coxiella burneti* that can cause fatal illnesses to the lungs. Dark biotechnological research might be abused to create pandemics and is a global threat. Terrorist acts include the use of biotechnological weapons such as the spreading of deadly pathogens.

Anthrax attack

In 2001 an anthrax attack in the USA, via a letter, proved to stem from Dr Bruce Ivins' US laboratory, which caused several deaths.[58] It is still unknown how this deadly pathogen escaped from the high-security laboratory (Steiner 2020: 61–62). However, it was later declared that Ivin was the sole culprit after committing suicide in 2008. This example proves how easily highly contagious biological agents can create disaster when used for the wrong reasons. It was a wake-up call for institutions and Biosafety Committees. Luckily, the anthrax attack did not involve multiple agents or modes of transmission, transmission to animals or the threat of global spread. It is also not a drug-resistant organism. It, however, alerted institutions and ethics committees to be more cautious about black technology practices.

[58] The anthrax attacks in the USA happened seven days after the 11 September 2001 terrorist attacks. Letters laced with deadly anthrax spores were anonymously sent to media companies and congressional offices. Five people died and seventeen others were infected. The source was traced back to the government's biodefense lab of the scientist, Bruce Edwards Ivins. He committed suicide before facing charges (NCBI, n.d.).

Black biotechnology uses pathogens to spread destruction deliberately and is considered the dark, unethical side of research activities for all the wrong reasons and to harm. Black biotechnology includes many different menace actions, for example, biological agents are engineered into more virulent forms that can cause mass destruction. Illness triggers can quickly artificially produce in the laboratory, which means a virus can be created. If this knowledge is abused, it can cause major disasters globally (Bronze, 2002: 316).

EBRECs should only approve responsible science and be aware of any possible illegal and unethical practices. Biosafety laboratories should be registered and monitored by an EBREC and have all biosafety measures in place. It includes protecting sensitive data to prevent the unauthorised use of genetic engineering of biological agents to enhance the virulence of pathogens. Evidence of black biotechnology on a pathogen should be immediately reported to the Biological Toxins and Weapons Convention (BTWC).

Violet biotechnology handles the compliance, ethical and philosophical issues regarding biotechnology and **considers ethical and moral issues in EBR,** such as germline manipulation, animal testing, cloning and assisted reproduction (Steiner, 2020: 53)**.** It deals with applicable laws and the legal aspects surrounding science as well as the moral and ethical principles regarding topics. It is also related to patents, publications, intellectual property and inventions devoted to solving problems and regulating scientific actions. Thus, it is biotechnology's governance through regulation and problem-solving and not biotechnology per se, but it remains an integral part of all biotechnology processes (Bhatia, 2018: 5; DaSilva, 2004).

Violet (or Purple) biotechnology can be seen as the governing or regulatory body, acting as a mediator for other branches of biotechnology (Steiner, 2020: 53–58). Scientific achievements are never only the work of one person. When one researcher formulates a theory, many other researchers continue with it. This can lead to ambiguity and controversy, creating a need for a regulatory body to act as the mediator.

The boundaries of research studies in EBR can become so vast that a regulating mechanism is needed. In the legal field, a researcher and the EBREC need to analyse if the extent and use of biotechnology in a research project are legal and which laws need to be implemented. In addition, another branch of violet (purple) biotechnology is the rules and regulations for publications in biotechnology.

Violet technology is devoted to resolving problems through regulation and forming a platform for discussion (CHEMIC, 2012: 815). The question remains if the current governance in this

complicated and extended biotechnology field is prepared to answer all the questions? Jonas Monast from the School of Law at the University of North Carolina indicated that biotechnology governance in the USA could not address all the new generation techniques and inventions. (Monast, 2018: 2436). If this is the case in a world-leading country such as the USA, it is understandable that other countries, and specifically South Africa, also struggle with proper governance.

APPENDIX D: RELEVANT ACTS, REGULATIONS & GUIDELINES

In South Africa, the following Departments regulate GMOs

1. **Department of Agriculture, Land Reform and Rural Development (DALRRD)**
   Applicable Legislation that governs all activities with GMOs:
   1.1 Genetically Modified Organisms Act No. 15 of 1997
   1.2 Genetically Modified Organisms Amendment Act No. 23 of 2006
   1.3 Genetically Modified Organisms Act Regulations No R. 120 of 2010

2. **Department of Health (DoH)**
   Other legislation controls the manufacture, importation and sale of foodstuff, disinfectants and cosmetics. The DoH accepted The Codex Alimentarius guidelines and principles as a policy for food safety requirements. The following are applicable acts:
   2.1 Foodstuffs, Cosmetic and Disinfectants Act No. 54 of 1972
   2.2 Foodstuffs, Cosmetic and Disinfectants Act Regulations No. R 25 of 2004

3. **Department of Environmental, Forestry and Fisheries Affairs (DEFF)**
   Applicable Legislation under DEFF:
   3.1 (NEMBA) National Environmental Management: Biodiversity Act No. 10 of 2004

   The South African National Biodiversity Institute (SANBI) monitors and reports potential environmental impacts of GMOs released into the SA environment as conferred by NEMBA. They also establish mechanisms for environmental impact assessment under NEMA (Environmental Management Act) regarding GMOs.
   The following legislation applies:
   a. *National Environmental Management Act (NEMA) No. 107 of 1998*
   b. *National Environmental Management Act Amendment No. 8 of 2004*
   c. *National Environmental Management Act Regulations No. R 385 of 2006*

   NEMA regulates activities, developments and products to ensure the sustainability of the environment as well as social and economic sustainability.

4. **Department of Trade and Industry and Competition (DTIC)**
   The act establishes national norms and standards for consumer protection and access to information. It also outlines GMO labelling requirements:
   4.1 Consumer Protection Act No. 68 of 2008: Section 24(6) pertains to GMOs
   4.2 Consumer Protection Act Regulations No. R 293 of 2011; Section 7 pertains to GMOs

5. **Other Resources and Guidelines**
   5.1 **DoH's** requirements are included in *The guideline document for working with GMOs under section 5.2 of the GMO Act*

   5.2 **DEFF:** *Environmental Risk Assessment Framework for Genetically Modified Organisms: A Guidance Document* and

Risk analysis of contained use research and development activities with genetically modified aquatic organisms.

5.3 **DSI:** Provides *the Bio-economy Strategy* to address future challenges and enabling an environment to encourage innovation for socio-economic development in South Africa.

5.4 **ASSAf:** The Academy of Science of South Africa promotes science for the benefit of the South African society and their mandate encompasses all fields of scientific enquiry. ASSAf represents South Africa in the international community of science and is recognised by the government. The following guidance documents are for reference:

5.4.1 The Regulatory Implications of New Breeding Techniques (2017)
5.4.2 The State of Biosafety and Biosecurity in South Africa (2015)
5.4.3 Policy Makers Booklet. Regulation of Agricultural GM Technology in Africa (2012)
5.4.4 GMOs for African Agriculture: Challenges and Opportunities (2010) part 1 & part 2

5.5 BIOSAFETY SOUTH AFRICA

The following are valuable documents and are available for easy reference when needed:

5.5.1 Procedure to register a facility for GM use
5.5.2 Risk Mitigating Strategies (RMS) for GM Products
5.5.3 Current practice and potential impact of in-field separation strategies for GM and non-GM maize
5.5.4 Maze and Bacillus thuringiensis Cry protein allergenicity
5.5.5 Application for authorisation to import GMO's intended for trial release in SA

(Biosafety South Africa, n.d.)

Click on the link below to access all the mentioned documents and information.

Relevant acts, regulations & guidelines

APPENDIX E: ADDITIONAL UNIVERSAL INSTRUMENTS

Other regional instruments, treaties and conventions worth mentioning include:

The UNESCO Recommendations on Science and Scientific Researchers was documented in 1974 to codify science's value systems and goals and how it should be protected and supported. This document was revised and adopted on 13 November 2017. It expanded the scope and reach of the former recommendation with an added monitoring procedure. The code also tries to assist with the building of scientific skills for developing countries. It informs adequate policies to ensure the responsible use of knowledge from all scientific fields (UNESCO General Conference 39 C/Resolution 85).

The UNESCO Declaration on Ethical Principles in Relation to Climate Change addresses the challenges and ethical principles that should be applied globally regarding climate change. The declaration is not a duplication, contradiction or re-interpretation of other notable documents, e.g. UN Framework Agreement on Climate Change, Kyoto Protocol or the Paris Agreement. The Kyoto Protocol and the Paris Agreement are both action documents in climate protection. The Kyoto Protocol was issued in 1997 and was the first legally binding document with obligations to maintain international climate protection. The Paris Agreement was a follow up in 2015, including a target to limit global warming. Countries should set reduction targets. Knowledge of these two documents can assist researchers in studies that strive to find solutions for this global disaster.

The American Biological Safety Association (ABSA) was founded in 1984 and was probably the first of its kind to promote “biological safety” as an essential principle.

The United Nations Environmental Programme (UNEP) has several functions, for example, the development of international environmental conventions. It also contributes to different codes of conduct, such as Code of Ethics, Climate Technology Network (CTN), Code of Ethics on the International Trade in Chemicals and many others. Global Frameworks from UNEP include:

- Implementing Consistent Ecological Risk Assessment of Pesticides for Sustainable Agriculture (IUPAC)
- Stockholm Convention on Persistent Organic Pollutants
- Rotterdam Convention
- Basel Convention on the Control of Trans-boundary Movements of Hazardous Wastes and their Disposal
- Vienna Convention for the Protection of the Ozone Layer

- Montreal Protocol on Substances that Deplete the Ozone Layer
- Chemical Weapons Convention
- U.N. Security Council Resolution
- The Rio Declaration on Environment and Development (1992)

These regulatory frameworks also aim to foster international scientific collaboration and to the contribution of risk assessment methodologies (SATORI, 2015: 16–17).

The Codex Alimentarius Commission addresses food safety, develops standards and guidelines for genetically modified foods.

The TRUST Project for Equitable Research Partnership is a collaborative effort and international network on global ethics governance to improve adherence to high ethical standards of vulnerable populations around the world. The TRUST Report guides community engagement in research following four values: fairness, respect, care and honesty. The values of “care” includes the consideration for environmental protection and sustainability in research ethics processes and frameworks for responsible research (Chatfield, 2018: 12). These values should be the cornerstone for equitable research between high-income countries and low- or middle-income countries in any discipline. They should be applied before, during and after any research study (Chatfield, 2018: 1–31).

The Engineering Code of Ethics **(Hederkodex), the Hippocratic Oath for Scientists,** and the Toronto Resolution are codes that formulate the researcher's ethical obligation.

The Uppsala Code is another well-known code developed in 1980 to protect the environment and find a way to fight against the threat of mass destruction weapons and focus on an individual scientist's responsibilities and people's protection, thus, a broad society focus (Science and Engineering Ethics, 2000).

The Code of Conduct for Responsible Nanotech Research. Long term consequences of new techniques, for example, nanotechnology, raised questions regarding the risk of unintentional releases of nanoparticles that can be highly toxic. The code of conduct invites the different stakeholders to act responsibly and cooperate to ensure that nanotechnology research is undertaken in the community in a safe, ethical and practical framework, supporting sustainable economic, social and environmental development (European Commission, 2009: 13).

These UNEP global frameworks also aim to foster international scientific collaboration and contribute to risk assessment methodologies (SATORI, 2015: 16–17)

- The Codex Alimentarius Commission
- The TRUST Project for Equitable Research Partnership
- The Engineering Code of Ethics (Hederkodex) – the Hippocratic Oath for Scientists.
- Toronto Resolution
- The Uppsala Code
- The Code of Conduct for Responsible Nanotech Research.

These universal instruments and frameworks are by no means a complete list but a starting point of the international statutory responsibilities in EBR and biotechnology.

APPENDIX F: ETHICAL CLEARANCE

ETIEKVRYSTELLING VERKLARINGSVORM

Naam van student	**Maricél van Rooyen**
Studentenommer	**22418547**
Graadprogram	**Mphil Applied Ethics**
Jaar van registrasie	**2019**
Titel van tesis / proefskrif	Environmental and Biosafety Research Ethics Committees: Guidelines and principles for ethics reviewers in the South African context
Departement	**Philosophy**
Studieleier / promotor	**Dr Johan Hattingh**
Mede-studieleier(s) / promotors [*indien van toepassing*]	

Ek verklaar hiermee dat:

- Ek **nie** data versamel of met individue gekommunikeer het by wyse van onderhoude, opnames, fokusgroepe, waarnemings, video-opnames, ens. nie.
- Ek **nie** toegang verkry het tot organisasies (instellings of ondernemings) se vertroulike data of inligting (insluitend argiefdata, kontaklyste of verslae) nie.
- Ek **nie** saamgewerk het met instellings (organisasies of ondernemings) wat my toegang gegee het tot fisiese (of finansiële) data wat gekoppel is aan individue, persoonlike rekeninge of inligting nie.
- Ek **nie** toegang verkry het tot enige databasisse of argiewe wat persoonlike identifiseerders (bv. name, ID-nommers, rekeningnommers, studentenommers, ens.) bevat nie; EN/OF toegang verkry het tot enige databasisse wat gekodeerde inligting bevat nie (d.w.s. waar kodes gekoppel aan persoonlike identifiseerders tot my beskikking was nie).
- Ek **nie** inligting of data versamel het wat in die publieke domein beskikbaar is MAAR as sensitief of potensieel sensitief beskou kan word nie (bv. data wat versamel is via sosiale netwerke of openbare profiele soos Twitter, LinkedIn en Facebook).

16/08/2021 Studenthandtekening

17 August 2021

Studieleier / promotor se handtekening — Datum

[Hierdie voltooide en getekende vorm moet saam met die tesis / proefskrif en ander stawende dokumentasie in ’n zip-vouer per e-pos aan Nicky Steenstra (nicky@sun.ac.za) by die Nagraadse Eksamineringskantoor gestuur word.]