UNIVERSITY OF CALGARY

Scoping the Literature for Synthetic Biology's Envisioned Products: Identifying Potential Impacts on the Lives of Albertans

by

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Abstract

Synthetic biology (SB) is an emerging field of biological research focused on the (re)design and construction of genetic devices and living systems for useful purposes. While the United States and Europe remain world leaders in SB, Alberta has also shown interest in the field. Through Alberta Innovates (formerly Alberta Ingenuity), the province has provided financial support for numerous Alberta-based undergraduates participating in the international competition in SB (iGEM) since 2006. Proponents assert SB could facilitate the creation of numerous biological products across a variety of sectors, such as medicine and the environment. If successful, they could provide enormous benefit for society. As with any powerful new technology, however, they also pose societal risks.

Previous studies have focused on identifying the bio-safety, security, and regulatory impacts of SB as a whole. None, however, have attempted to systematically catalogue what products have been envisioned since the field's emergence. Further, no previous studies have assessed the potential implications that an envisioned SB product might someday have on the social well-being of a population outside the developing world. This study addressed these knowledge gaps by a) scoping SB discourse for the field's envisioned products, and b) developing and implementing an upstream product assessment framework to identify the potential implications that an 'exemplar' product of relevance to Alberta (*re-designed microbes that produce bio-butanol transportation fuel*) might have on the social well-being of its citizens.

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"Perseverance is not a long race; it is many short races one after the other"
- Walter Elliot

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DEFINITION OF KEY TERMS

Term	Definition
Abstraction (The engineering principle)	Unnecessary details ought to be ignored in the engineering of complex systems. In the engineering of biological systems, abstractions refers to classifying the system first into: parts, followed by devices, then systems, which are ultimately contained within a 'chassis' (1,2)
Benefit	A good that contributes to the well-being of an individual and/or given community (3)
Biomedical Health	Within the context of the biomedical model of health, the absence of disease. Only physical interventions, such as the administration of medication, can be used to cure or treat the bodily machine (4,5)
Decision Makers	Individuals responsible for the creation of policies in the government, science, and other institutions
Determinants of Health	Factors that together contribute to the state of health and well-being of a population or individuals (6) (*see Social Determinants of Health)*
Discourse	Written or spoken communication (or debate) (7)
Document	A written, printed, or electronic piece of matter that provides information or evidence or that serves as an official record (8)
Emerging Technology	A technology that is not yet widely commercialized or adopted, but that is expected to have a substantial impact in the next 5-10 years (9)
Ethics	The explicit, philosophical reflection on moral beliefs and practices (10)
Foresight	Looking forward; making a judgement or prediction about a future event that may or may not occur
Genetic Engineering	The act of artificially manipulating an organism's genetic code. Its focus normally lies on the manipulation of an individual gene or gene pathway (11,12)
Genome	The complete set of genetic material found in an organism, which includes all of its genes (13)
Grey Literature	A body of material such as reports, theses, and conference proceedings that are not readily available through conventional channels because they are neither widely published nor widely distributed (4)
Grounded Theory	A qualitative research methodology that entails a process of analytic induction through which meanings are inferred from the data collected. It is generally concerned with the discovery of hypotheses from texts (4)
Health	A state of complete physical, mental, and social well-being and not merely the absence of disease or infirmity (14)
Health Technology Assessment	A field of evaluation that provides information about a technology's efficacy, safety, and cost-effectiveness (15,16).
Modularity (The engineering principle)	Systems are, or ought to be, composed of standardized units or dimensions for ease of construction, flexible arrangement, and variety in use (2) **(Cont'd)**

Term	Definition
Morality	Beliefs and practices about good and evil that guide human behaviour (10)
Nanotechnology	An emerging technology that deals with the creation and manufacturing of electronic circuits, devices, and machines with dimensions within the range of one-billionth of a meter (17)
Population Health	The health outcomes of a group of individuals, including the distribution of such outcomes within the group (18)
Protocell	Minimalistic “chemical life-like ensemble(s)” that can grow, reproduce, and evolve; akin to the cellular precursors believed to exist at the beginning of life (19,20)
Renewable Energy	Energy that cannot be depleted with time, unlike other sources that are exhaustible, such as energy derived from fossil fuels.
Risk	A potential, but not precisely knowable, harm (21); an unwanted event that may or may not occur (22)
Risk Assessment	A process of characterizing and quantifying risks that is used to inform decisions made under a state of uncertainty (23). Conventional (quantitative) risk assessment is a scientific process consisting of: (i) hazard identification, (ii) hazard characterization, (iii) exposure assessment, and (iv) risk characterization. It also involves characterizing and quantifying uncertainties (23,24).
Risk Communication	The interactive exchange of information and opinions throughout the risk analysis process. It includes the explanation of risk assessment findings and the basis of risk management decisions (25)
Risk Management	The process of weighing policy alternatives in consultation with interested parties. Risk assessment and other legitimate factors are considered during this process during which appropriate prevention and control options are selected (24,26)
Social Determinants of Health	A subset of determinants of health that generally focus on the “economic and social conditions that govern people’s lives” (27)
Synthetic biology (SB)	The design and construction of new biological parts, devices and systems that do not exist in the natural world, and the redesign of existing biological systems to perform specific tasks (28)
Technoscience	The hybridization of technology and science (29,30)
Well-being	A dynamic state of physical, mental and social wellness. It has been viewed as the result of four key factors over which an individual has varying degrees of control: human biology, social and physical environment, health care organization (system), and lifestyle (31)
Xenobiotic	A substance (typically a chemical) that is foreign to the body and/or an ecological system (32)

CHAPTER 1: THESIS INTRODUCTION

Synthetic biology (SB) is a rapidly emerging field of biological research developed from the knowledge and principles of three scientific and technological domains: molecular biology, information technology, and engineering (11,33,34). Although the term has appeared in scientific literature for more than a decade, no single internationally recognized definition for SB exists (35,36). This study uses a 2007 report, which defines the field as 1) the design and construction of new biological parts, devices, and systems that do not exist in the natural world and 2) the re-design of existing biological systems to perform specific tasks (28).

In general, SB practitioners aim to make the engineering of biological molecules, devices, and systems scalable and predictable. To date, their research has resulted in the design and creation of several practical genetic circuits, the re-design of yeast cells that produce the anti-malarial drug Artemisinin, and the creation of the first self replicating semi-synthetic bacterial cell (35,37-39). In the more distant future, proponents assert the field could facilitate the creation of numerous products for use across a variety of sectors from energy to health and the environment. Some examples of these product visions include: re-designed microbes that produce bio-fuels, medicines and food ingredients (40,41), viruses, bacteria, and 'regulatory circuits' (re)engineered to identify and destroy cancer cells within the body (40,42), and (re)engineered microbes and plants that identify and destroy pollutants (43).

1.1 PROBLEM STATEMENT

Envisioned SB products have an enormous potential to impact many aspects of our lives, from the medicines and fuels we use, to the food we eat and the environment in which we live. Proponents stress these products could someday provide enormous benefit for society. Like any powerful new technology, however, they also pose risks, including the potential for harmful consequences for the environment, human health, and social well-being (43-45). Given this potential, there is a need to investigate the field to better understand what products may be developed in the future, and the potential impact they might have on populations, or processes, of interest.

SB has existed for more than a decade, yet no previous research has attempted to systematically identify and catalogue what products have been envisioned since the discipline's emergence. In addition, there is a lack of methodological detail about how to proactively assess an envisioned SB product in order to understand how that product might someday impact the social well-being of a particular population of interest. This work fills these knowledge gaps by **a)** scoping the literature for SB product visions and **b)** developing and implementing an upstream SB product assessment to identify the potential implications that an 'exemplar' product of relevance to Alberta might have on the social well-being of its citizens.

1.2 Research Questions

The central research question examined in this study was: *how might SB's envisioned products impact the lives of Albertans?* Over the course of the research process, two 'subsidiary' research questions evolved and helped refine and focus the scope of the research. These included:

1) What SB products have been envisioned since the year 2000?
    1a) What is the nature of that discourse?
2) Of SB's envisioned products, which might be of particular relevance to the Province of Alberta?
    2a) How might an 'exemplar' product of relevance to Alberta impact the social well-being of its citizens?

1.3 Significance of the Study

This study will contribute to a better understanding of SB's potential by identifying the possible directions its product developments might take in the future. It will also contribute knowledge about the potential implications that an envisioned SB product might have on the social well-being of Albertans. Hence, this research is of significance to future researchers interested in studying SB, particularly, academics in the fields of social science and emerging technology. This study will also be beneficial to Alberta-based decision makers because it identifies the possible implications that an envisioned SB product of relevance to their province might someday have on the social well-being of their citizens.

1.4 Definition of Terms

For a clearer understanding of important vocabulary used in this study, definitions of key terms have been listed in alphabetical order, beginning on page x. All terms underlined throughout this thesis are listed in that location.

1.5 Scope and Delimitations

The scope of SB is broad. It encompasses several branches of science and technology, is becoming increasingly popular around the world, and its envisioned products are poised to reach numerous application domains. Indeed, many aspects of the discipline cannot be fully analyzed in a single research study. As such, the scope of this study was delimited in the following ways:

Scoping Review:

- Information sources were limited to 1) English-language documents: 2) published between 2000-2010 inclusive, 3) available in electronic format and 4) readable in ATLAS.ti qualitative content analysis software

Identification of an Alberta-Relevant Product:

- This study limited its focus to the Province of Alberta. As such, only one Alberta-relevant product, among many, was chosen for assessment

Upstream Product Assessment:

- A wide range of potential stakeholders were initially identified, however, the assessment was limited to Alberta's general public (as bio-fuel consumers) and the province's farmers (as feedstock producers)
- The source of information used to complete the assessment was limited to published documents

1.6 THESIS STRUCTURE

This thesis is organized into seven remaining chapters. The following chapter (two) provides an introduction to the field of SB. Chapter three covers the conceptual framework, and in chapter four the results of a scoping review of literature relevant to the research topic, are presented. In chapter five, the methodology used to achieve the research aims is explained and in the following chapter (six) the study's findings are presented. Chapter seven presents a discussion of those findings. In the final chapter (eight), the study is concluded by summarizing key findings, discussing limitations, and suggesting areas for further research. Appendices have been provided following a list of references, which incorporate additional information on some of the topics introduced in the thesis.

CHAPTER 2: INTRODUCTION TO SYNTHETIC BIOLOGY

The preceding chapter introduced the overall study. The current chapter presents a more detailed introduction to the study's central topic area: **synthetic biology**. Given that the field is novel, and many people are not aware that it exists (46,47)[1], a solid knowledge foundation of SB was needed to provide sufficient context for the information presented in subsequent chapters.

This chapter begins with a discussion of SB's historical roots (section 2.1). Next, the chapter discusses how the field is defined, its practical influences, and the five methodological approaches currently used to perform SB research (sections 2.2-2.4, respectively). Following these sections, an overview of the geographical distribution of SB research activity is discussed (section 2.5) and a brief description of the discipline's key accomplishments to date are presented (section 2.6). The chapter ends with section 2.7, which summarizes the chapter and introduces the following chapter (three).

2.1. SYNTHETIC BIOLOGY'S HISTORICAL ROOTS

The birth point of SB is generally marked by the creation of the first man-made gene regulation networks[2] in the year 2000 (11,33,34). While the discipline's emergence is normally attributed to these practical accomplishments, the *desire* to build biological systems was, in fact, conceived much earlier. When longstanding theories about spontaneous generation were largely abandoned by the 19th century scientific community, a *synthetic* approach to biology became envisioned. At the time, it was hoped that biological synthesis would someday

[1] A 2010 survey found that only 22% of the United States' general public were aware that SB existed (46). A similar United Kingdom (UK)-based survey in 2009 revealed that only about one quarter (22%) of the UK general public surveyed had heard about it. Further, only 10% of respondents who had actually heard about the discipline revealed they did not know what it meant (47).

[2] Gene regulation networks are responsible for governing the rate of protein synthesis within cells. In 2000, two such networks were synthesized using SB techniques: the on-off 'toggle switch' and the 'repressilator' (11,33).

complement the traditional 'top down' or 'deconstructive' approach to biological analysis (*e.g.* dissection) (48,49). Indeed, the conceptual foundation of modern day SB was born from the work of scientists over a century ago.

In 1906, Jacques Loeb, a German-American biochemist, stated that the *synthesis of life* itself was the ultimate goal of biological understanding. Although the term 'synthetic biology' was not explicitly used to describe this goal, the term did emerge in scientific literature six years later. In his 1912 book titled "La Biologie Synthétique" (50)[3], Dr. Stéphane Leduc explained that biological synthesis would most certainly advance biology as a discipline (30,51).

The paradigm-shifting ideas brought forth by Loeb and Leduc helped lay the conceptual foundation of modern-day SB (50-52). Certainly, the notion that the biological synthesis would help advance our understanding of life remains at the cornerstone of modern SB research (30). The *practice* of SB, however, would not have been possible without the emergence of the practical tools of molecular biology, such as recombinant DNA technology. Since their emergence in the 1960's and 70's, the tools of molecular biology have provided scientists a more in-depth understanding of genetic replication, regulation, and manipulation. Indeed, they also serve as the fundamental tools needed to carry out SB research (48,53).

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[3] Many cite Barbara Hobom's use of the term Synthetic Biology in her 1980 article "Surgery of genes. At the doorstep of synthetic biology" (523) as the earliest explicit use of the term in the scientific literature (35,201,416). While Dr. Hobom used 'Synthetic Biology' to describe her experimental techniques, she used the term synonymously with genetic engineering (416).

2.2 DEFINING SYNTHETIC BIOLOGY

Although the term has appeared in literature for more than a decade, the discipline continues to evolve so rapidly that no current internationally accepted definition exists (54-58). Some of the most commonly cited definitions, however, have been listed in Table 2.1.

TABLE 2. 1 COMMONLY REFERENCED DEFINITIONS FOR SYNTHETIC BIOLOGY

Source (*Location*)	**Definition**
Synthetic Biology. Org (*Internet*) (59)	Synthetic biology refers to both: a) the **design and fabrication** of biological components and systems that do not already exist in the natural world and b) the **re-design and fabrication** of existing biological systems
The Royal Society (*United Kingdom*) (60)	Synthetic biology is an emerging area of research that can broadly be described as: • The **design and construction** of novel **artificial** biological pathways, organisms or devices, or • **The redesign** of existing **natural** biological systems
Extreme Genetic Engineering: An Introduction to Synthetic Biology (*Canada*) (28)	Definition: Synthetic Biology • The **design** and **construction** of new **biological parts**, **devices** and **systems** that do not exist in the natural world and also • The **redesign of existing biological systems** to perform specific tasks

* According to the Woodrow Wilson International Center for Scholars' 'Synthetic Biology Project' (36)

As highlighted (bold) in Table 2.1., across some of the most commonly cited definitions of SB, two common elements generally exist: SB research encompasses: a) **the design and construction** of biological pathways, devices, and organisms that **do not exist in nature** and b) **the re-design** of naturally-occurring biological systems, to perform specific tasks.

While some have referred to the discipline as "extreme *genetic engineering*" (28), due to the perceived negative social implications associated with the term genetic engineering, SB practitioners have been keen to distinguish it from their field (57). In much the same way, the discipline has acquired a variety of synonyms largely in an attempt to avoid the term 'synthetic', believed to carry with it negative connotations of un-naturalness (57). Some of the most common synonyms include: constructive biology, intentional biology, natural engineering, genomic alchemy, and synthetic genomics (28,55,57,61). With the exception of 'synthetic genomics'[4], however, none have become widely adopted (57).

2.3 SYNTHETIC BIOLOGY'S 'PRACTICAL' INFLUENCES

As noted by Boldt & Muller (2008), SB's aims reach far beyond modifying one or two genes in simple organisms (62). Instead, SB practitioners aim to design and engineer entirely new metabolic pathways, and even completely novel genomes, in organisms to fulfill specific tasks (62). To achieve these ambitious aims, practitioners draw upon the tools and techniques made available by previous achievements in science and technology. As such, the discipline can be described as a multidisciplinary technoscience, whose evolution continues to be inspired by the convergence of three main scientific and technological domains: molecular biology, engineering, as well as information and communications technology (29,30).

Given the diverse nature of SB's influences, it is clear that the discipline's practitioners view life, and the manner in which it should be studied, differently than most mainstream biologists (63). In the sub-sections that follow, each of the field's three scientific and technological influences is explained in further detail.

2.3.1 MOLECULAR BIOLOGY

Molecular biology is the study of the composition and functional mechanisms of genetic molecules, such as DNA and RNA. Molecular laboratory methods emerged in the 1960's and 70's when biologists first 'cut and pasted' single pieces of DNA into living cells,

[4] Some define synthetic genomics as a sub-discipline of SB; one that focuses narrowly on the synthesis and assembly of genomes (524). In this study, however, no such distinction has been made.

resulting in an expansion of their natural function (34,64,65). Some of the most well-known molecular techniques born from molecular biology include recombinant DNA technology and genetic engineering. Recombinant DNA technology is an umbrella term that refers to the introduction of a single gene into a living cell, whereas genetic engineering generally refers to the act of artificially manipulating an organism's genetic code. Its focus normally lies on the manipulation of an individual gene or gene pathway (11,12). As a genetic discipline, SB uses molecular methods to design and assemble DNA-based devices that perform novel functions. SB practitioners have also recently drawn upon molecular methods to create entire microbial genomes (66). In the future, some SB practitioners aim to use these techniques to produce novel organisms with novel traits that have never existed before (67).

2.3.2 ENGINEERING'S UNDERLYING PRINCIPLES

Common to many explanations of SB is the notion that the discipline applies the fundamental principles of engineering, such as <u>modularity</u> and <u>abstraction</u>, to the basic components of biology (36,53,55,68). Synthetic Biologist Dr. Drew Endy heavily endorses this "engineer's approach to biology" (69) and has described four main challenges of biological systems within this context: biological complexity, difficulty in standardization, mutation, evolution, and the tedious and unreliable nature of biological construction (55,70).

2.3.3 INFORMATION AND COMMUNICATIONS TECHNOLOGY

Information technology is an umbrella term that refers to the "acquisition, processing, storage and dissemination" of information using a combination of computing and telecommunication micro-electronics (71). The concepts underlying this field of study, especially the standardization and characterization of interchangeable components, have influenced the approaches taken to carry out SB research (37,72). Indeed, many view the ultimate goal of SB as the construction of individual, standardized, components (genetic circuitry) that can be combined in a variety of ways to produce desirable 'machines' or 'devices' (37,72). It is unlikely that future biological circuits would achieve the so-called computing power of today's digital electronics. As noted by Lu *et. al.* (73), however, they might help increase the "reliability and programmability of biological behaviours" (73).

2.4 The Five Main Approaches to Synthetic Biology Research

SB practitioners are unified by similar goals, but they do not necessarily approach their research in a uniform manner. Within SB literature, four main methodological approaches are discussed (19,20,74-79), and include:

1) The Construction of DNA-based Devices
2) Genome Engineering
3) Bottom-up and Top-down SB:
    a) Construction of Minimal Genomes (Top-Down)
    b) Synthetic Protocell Biology (Bottom-Up)
4) Chemical Synthetic Biology

Gaining a fundamental understanding of the approaches taken to 'engineer life' can help solidify an understanding of SB as a discipline. In the sub-sections that follow, each of these approaches is explained in further detail.

2.4.1 Construction of DNA-based devices

In the 'device construction' approach to SB, practitioners attempt to assemble genetic 'parts' into larger circuitry for specialized application and rely heavily on the foundational principles of engineering and information technology to accomplish their tasks (80-82). Perhaps not surprisingly, many DNA device practitioners conceptualize cells as multifaceted *computing machines* containing *programmable material*, which can be modified to perform functions dictated by the *programmer* (63,83,84). This approach has been fundamental in advancing SB research, mainly because the approach has driven gene synthesis to become faster and more reliable (55,76,85). Dr. Drew Endy, the co-founder of the Registry of Standard Biological Parts and the undergraduate International Genetically Engineered Machines (iGEM) competition (see section 2.6.2) exemplifies this approach (86-88).

2.4.2 GENOME ENGINEERING

Genome engineers attempt to re-design the existing genetic material within organisms to create novel metabolic pathways that can be used for specified purposes, such as the production of medicinal chemicals (76). Beyond manipulating single genes, practitioners following this approach aim to engineer several genes to work together as one unit, much like "transistors wired in a circuit" (89). This approach is exemplified by Dr. Jay Keasling who, in 2003, announced the successful re-engineering of *Saccharomyces cerevisiae* (brewer's yeast) to make it capable of producing a chemical precursor to Artemisinin, a costly anti-malarial compound (90,91)[5]. For this achievement, Discover Magazine named him "2006 Scientist of the Year" (92).

2.4.3 'BOTTOM-UP' AND 'TOP-DOWN' SYNTHETIC BIOLOGY

The terms 'bottom-up' and 'top-down' are commonly used to describe a variety of SB research approaches (76,77,93). In this study, their use is limited to the context of minimal genome and synthetic protocell construction. According to Rasmussen *et al.* (94) and Bedau (93), the top-down approach to SB involves the systematic reduction or minimalization of an organism's genetic material. This is done by systematically removing the non-essential genetic elements from an organism's genome (53,93-95). By contrast, the bottom-up approach to SB

[5] Endy does not believe this is an accomplishment of Synthetic Biology, but rather considers the feat a simple extension of metabolic engineering (90).

involves the design and creation of novel organisms, complete 'from scratch'. This is done by assembling the organism's genome, piece by piece, from its basic chemical components (93). Dr. J. Craig Venter's recent achievements in top-down and bottom-up 'synthetic genomics' are, arguably, the most widely discussed breakthroughs of the discipline today. As such, they are discussed in further detail in the sections that directly follow.

Top-down SB: The Construction of Minimal Genomes

The laboratory team of J. Craig Venter has made significant progress in determining the fewest number of genes necessary to support the life of a bacterial cell (65,93,96-98). Termed the 'minimal bacterial genome' in his 2007 United States patent application (US #20070122826 (99)), Venter and colleagues successfully created the first viable genetically reduced version of *Mycoplasma genitalium*. This minimal cell, which Venter referred to as *Mycoplasma laboratorium*, was a partially synthetic bacterial species, which continued to live freely, grow, and replicate in the laboratory (62,98,99). After the successful creation of *M. laboratorium*, Venter's team decided to change their approach to synthetic genomics research and pursue the creation of synthetic protocells. Using the top-down approach to SB, Venter aimed to design and engineer a minimal genome, completely from scratch, and insert it into a 'naked cell' with the hopes that it would live freely and replicate (98).

Bottom-up SB: Synthetic Protocell Biology

Venter and his team undertook a variety of steps in their quest to create the first man-made protocell. First, the team successfully transplanted genetically reduced versions of the *Mycoplasma mycoides* genome into genetically-void *Mycoplasma capricolum* cells (100). Based on a number of criteria, Venter's team verified the transplantation had indeed resulted in the creation of cells that were characteristically identical to *M. mycoides* (100). Next, the team synthesized the minimal genome completely from scratch, using a computer, a DNA sequencing machine, and yeast cells, which were ultimately used to assemble the genome. Once successfully assembled, Venter's team transplanted the synthetic genome into a *M. capricolum* host, creating what some refer to as the very first self-replicating bacterial protocell: *M. mycoides* JCVI-syn 1.0 (38,101).

2.4.4 CHEMICAL SYNTHETIC BIOLOGY

The 'chemical' approach to SB refers to the "synthesis of chemical structures alternative to those present in nature" (102). Practitioners who use this approach to SB envision a future where biological systems can be constructed from un-natural (non-DNA) nucleic acids, sometimes referred to as xenonucleic acids (XNA) (30,32,103). Schmidt (32) asserts <u>xenobiotic</u> organisms could indeed be used as a biosafety tool because, although future xenobiotic organisms might act like natural life forms, their genetic framework would be fundamentally different. As such, the exchange of genetic information between natural and xenobiotic organisms could be prevented.

2.5 SYNTHETIC BIOLOGY... GEOGRAPHICALLY SPEAKING

Based on the number of scientific publications and university courses on the discipline, in addition to the level of scientist involvement and available funding opportunities, the United States currently dominates SB research (43,104-107). Indeed, compared to other countries such as Japan, Israel, China and Canada where SB research is still in its formative years, in the United States, the field is already well-established and flourishing (104). Owing to the country's early lead in the field, Zhang (107) predicts the country will play host to the emergence of the world's first SB products.

From the year 2000 to 2005, SB research took place almost exclusively in two main geographical clusters on the American East and West Coasts (108). Since that time, research in the field has expanded throughout the rest of Europe and had has played an increasingly important role in the United Kingdom (UK). Indeed, this country currently posts the second strongest academic position in the discipline (108). Although, to date, the UK has not focused on the industrialization of SB, the country has become particularly dominant in the production of reports related to its governance (107).

Although currently not as dominant a player in the field as the United States and United Kingdom, SB has become an increasingly popular topic of interest in Canada. This country currently hosts the Ottawa-based Erosion, Technology, and Concentration (ETC) Group, a non-governmental technology watchdog organization frequently cited in American and European SB press. The Canadian federal government has also shown interest in the discipline. In 2006, Health Canada held a National Science Forum that included a discussion about the discipline's future in Canadian health and science research (109). Three years later, the organization's Health Products and Food Branch published a report in which SB was listed as an example of a 'horizon technology' that should be responsibly encouraged (110). Agriculture and Agri-food Canada has also expressed interest in the discipline. In 2010, SB was recognized as a discipline that would likely contribute to an enhanced understanding of the building blocks of life (111).

2.6 Synthetic Biology's Landmark Accomplishments

As a discipline, SB remains in its infancy, although several key accomplishments have been realized since its emergence in the year 2000. As discussed previously, perhaps the most well-known accomplishments have emerged from the American laboratories of Drew Endy, Jay Keasling and J. Craig Venter. Other important milestones, however, such as those shown on Figure 2.1 have also contributed to driving SB forward as a discipline. It is important to note that the items listed on Figure 2.1 (following page) are not exhaustive, but rather, they represent some of the most widely discussed milestones and events in SB's history to date.

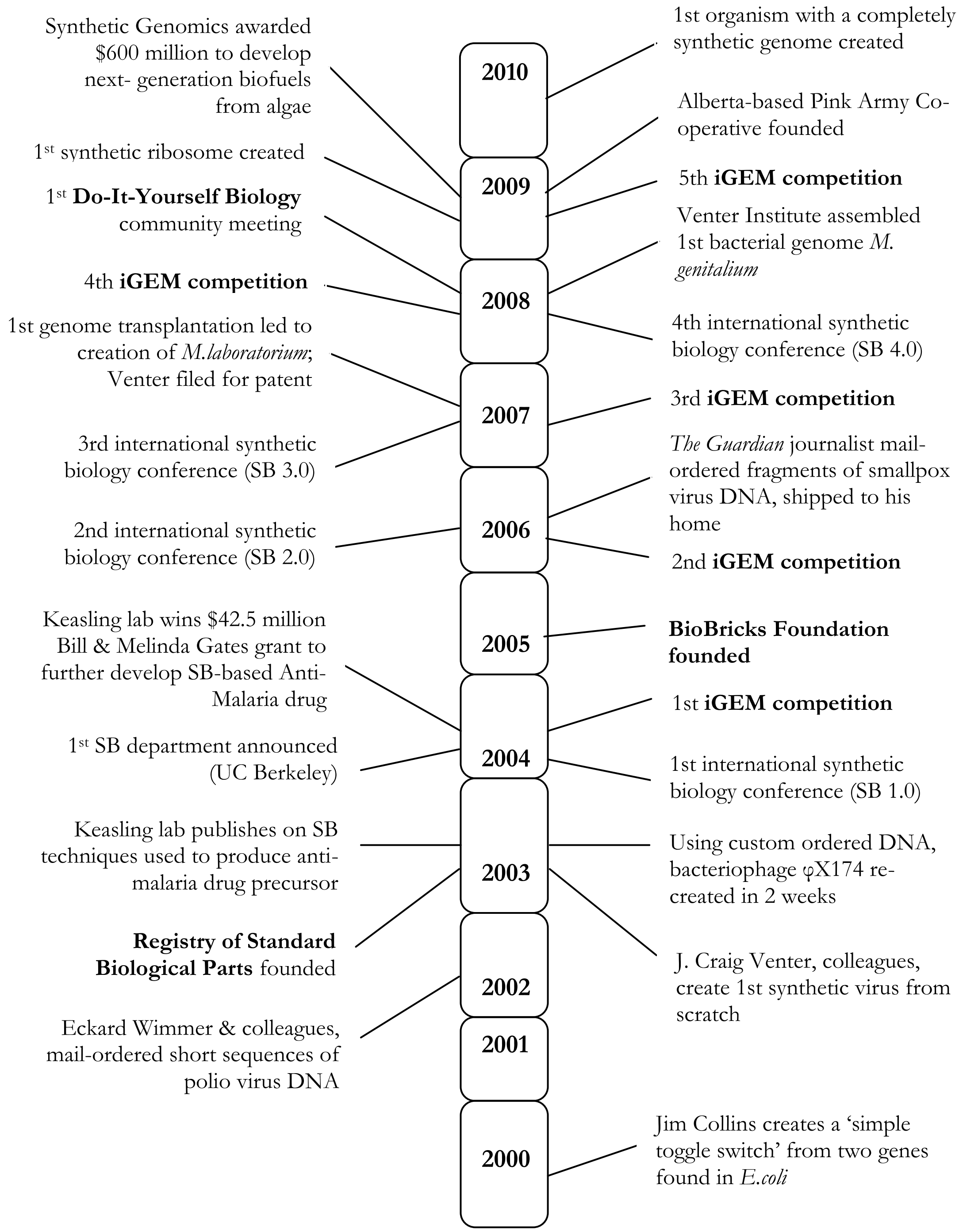

FIGURE 2. 1 MAJOR MILESTONES IN SYNTHETIC BIOLOGY'S DEVELOPMENT (2000-2010)

In sub-sections 2.6.1-2.6.4 (directly as follows), the milestones and events that have been **bolded** on Figure 2.1 are described in further detail.

2.6.1 THE REGISTRY OF STANDARD BIOLOGICAL PARTS

The Registry of Standard Biological Parts, co-founded by Drew Endy in 2003, is a continuously expanding open source database or catalogue of BioBricks (http://partsregistry.org/) (86). Sometimes referred to as 'DNA lego', BioBricks are standardized DNA building blocks that consist of individual genes and gene parts with defined structure and function. They are designed to be incorporated within the existing genetic circuitry of living cells to produce novel biological systems with unique functions (53). Thousands of distinct 'parts' are contained in the database today, all of which are grouped categorically based on function (*e.g.* protein coding, signalling, and cellular feedback) (112).

In keeping with its open source mandate, the information contained in the Registry's database is freely available for anyone who wishes to access it. Further, anyone can modify and improve the information contained within the catalogue (108). As such, it serves as a resource for academic research laboratories, Do-it-Yourself biologists (see section 2.6.3), and International Genetically Engineered Machines (iGEM) teams (86,113).

2.6.2 INTERNATIONAL GENETICALLY ENGINEERED MACHINES COMPETITION

The iGEM competition is the premiere international undergraduate competition in SB. It was born of a month long "Independent Activities Period" (113) project class at the Massachusetts Institute of Technology in 2003 wherein students were required to re-design cells with the ability to 'blink' (113-115). In the summer of 2004, the class grew into an official competition, with five teams having participated (113). Since that time, participation has dramatically expanded to include 130 international teams in from across the globe in 2010 including the United States, Canada, Asia, Europe, Latin America, and Africa (116).

iGEM teams can be distinguished into three main, yet overlapping, types or 'pillars' of competition: wet-laboratory, modeling, and human practices. The overall objective of wet-laboratory projects is to design and construct DNA-based biological parts and/or devices and incorporate them within living cells. Teams are provided a kit of BioBricks from the Registry of Standard Biological Parts and are required to use those parts, supplemented by BioBricks of their own design, to build novel genetic machines (86,112,114,117). Modeling teams focus on creating mathematical models and *in silico* simulations of BioBrick parts and devices in an effort to describe their function and operation (118). In recent years, the competition has broadened its aim to include projects that focus on ethical and social reflection (119). This pillar, which is referred to as 'human practice', requires teams to "find a new way to help human civilization consider, guide, and address the impacts of ongoing advances in biotechnology" (118).

Several projects born of iGEM have gained popularity in the media and academic circles and some have resulted in academic publication (91,120). Many teams have chosen to use *Escherichia coli* bacteria as their microorganism host of choice and have achieved a variety of successes in re-engineering the organism's genetic circuitry for a variety of specialized tasks. Key examples include successfully re-wiring *E. coli* with the ability to respond to light, produce pigments, and detect environmental toxins such as arsenic in contaminated water (91,115).

2.6.3 The BioBricks Foundation

The BioBricks Foundation was co-founded by Dr. Drew Endy and colleagues from various American academic institutions in 2005[6] (121). This non-profit, community-driven, organization is dedicated to ensuring that standard biological parts (BioBricks) remain freely available for open development, use, and sharing (122,123). The Foundation is currently working toward the development of a legal framework, which it refers to as the 'BioBrick Public Agreement' (115,122,124), to help facilitate their aim to enable "the free exchange and use of standard biological parts" (124).

2.6.4 Do-it-Yourself Biology

Do-it-Yourself Biology (DIYBio), the "institution of the amateur [biologist]" (125,126), is a growing organization that aims to make the practice of SB accessible for "citizen scientists, amateur biologists, and biological engineers" (125). Inspired by iGEM and the Homebrew Hacker Computer Club[7], DIY Biologists set up make-shift laboratories in their kitchens, basements, and garages and attempt to modify the genetic composition of life- often with no formal training and few resources (127). Proponents of the DIYBio movement maintain garage biology can be undertaken safely, while others worry 'biohacking' poses a danger to public health and the environment (127,128). The community's first official meeting took place in 2008 (see Figure 2.1).

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[6] Based on information provided on the BioBricks Foundation Website (121). This date is contradicted, however, by a 2009 article published in Nature Biotechnology, which reported the organization was founded one year earlier (115). Information obtained directly from the Foundation's Website was considered most accurate, and thus, the year 2005 is reported.

[7] A group of amateur computer and electronics enthusiasts in the 1970's and 80's who created make-shift computer factories in their garages. Their activities played a vital role in creating the world's first personal computers (126).

2.7 CHAPTER SUMMARY AND MOVING FORWARD

This chapter presented a broad overview of SB as a discipline. Now that SB has been explored in greater detail, this thesis moves forward to chapter three, wherein the basis of thought, and courses of action, required to address the central research question are delineated.

CHAPTER 3: CONCEPTUAL FRAMEWORK

The previous chapter provided a brief introduction to the emerging field of SB. The present chapter builds upon that knowledge foundation by presenting the study's overall conceptual framework; *i.e.*, the basis of thought and preferred courses of action employed to address this study's central research question.

3.1 INTRODUCTION TO THE CONCEPTUAL FRAMEWORK

As illustrated in Figure 3.1, this study's *initial* conceptual framework was comprised of three interlinked dimensions. The first two dimensions, represented by dashed Boxes A and B, served as the initial operational steps required to address the central research question (Box C).

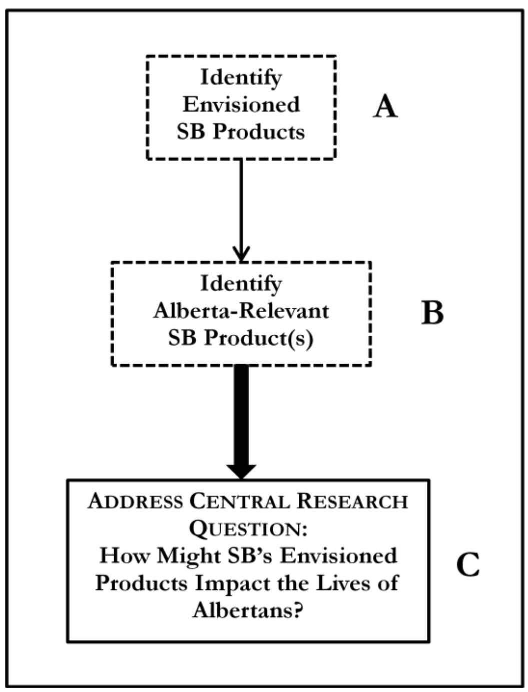

FIGURE 3. 1 A CONCEPT MAP ILLUSTRATING THIS STUDY'S INITIAL CONCEPTUAL FRAMEWORK

Each of the framework's dimensions was developed using relevant information identified through a series of focused literature scans. As such, over time, each dimension became more elaborate as the framework's development progressed. In the end, this process allowed for the creation of a *final*, more detailed, conceptual framework (Figure 3.5).

In sections 3.2-3.4, the process used to develop the framework is explained. Directly following this, section 3.5 presents the study's final conceptual framework, wherein each of the 'elaborated' dimensions was combined to form a more detailed concept map (129). The chapter concludes with a description of the study's philosophical underpinnings (section 3.6) and a declaration of this researcher's inherent perspectives on the study topic (section 3.7). The chapter is summarized in section 3.8.

3.2 DIMENSION ONE: IDENTIFYING ENVISIONED SB PRODUCTS

As a first step in the research process, it was necessary to gain an overall sense of what *specific* SB products had been *envisioned* since the discipline's emergence in the year 2000. Specifically, this author was interested in identifying SB products that were not extensively developed or marketed during the time this study was undertaken[8]. As discussed in chapter four (see section 4.3.1), a scan of scientific and grey literature revealed a gap in knowledge within this context. In sum, across the literature identified, many studies discussed the broad application areas wherein the discipline might someday become important (*e.g.* the environment or medicine). Others presented simple examples of specific products that might someday become realized (*e.g.* cancer scavenging microbes). No studies, however, endeavoured to systematically identify or map the breadth of SB product visions made over time (104,130-

[8] In this thesis, these are described using the terms 'product visions' and 'envisioned products'

132). After consulting with the supervisory committee, this researcher concluded that a 'scoping' review (133) of SB discourse could be employed to help fill this knowledge gap.

As illustrated in Figure 3.2, the term 'discourse' generally refers to spoken and written communication. In this study, however, only written discourse on SB was of interest[9]. Indeed, this researcher assumed that a broad inventory of SB's envisioned products could be obtained by examining the content of documents. As noted by Miller & Alvarado (134) documents are rich sources of data that are actively produced, exchanged, and consumed within society. As such, an analysis of their content could result in novel insights being gained that might not be accessible any other way (135).

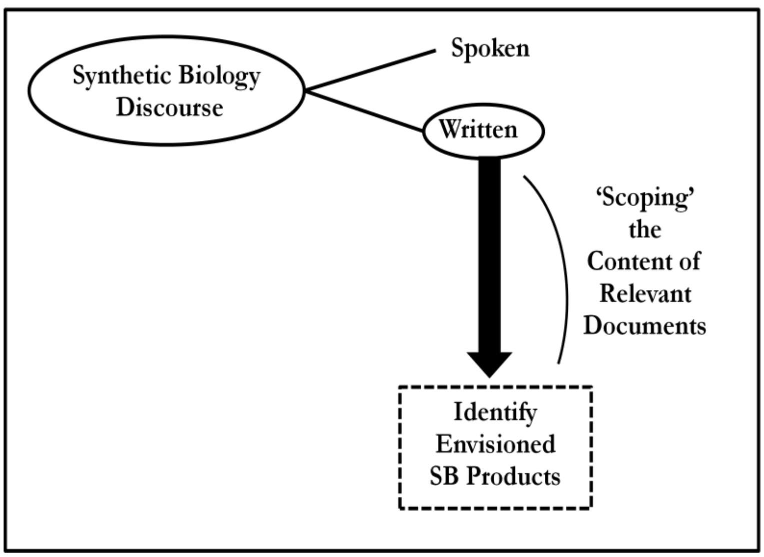

FIGURE 3. 2 THE CONCEPTUAL BASIS OF IDENTIFYING ENVISIONED SB PRODUCTS

3.3 DIMENSION TWO: IDENTIFY AN ALBERTA-RELEVANT PRODUCT(S)

Geographical areas- both large and small- can be quite diverse in terms of their overall economic, scientific, and technological landscape (136). As such, some SB product visions may be of greater interest and priority to a particular region of interest than others. Because this

[9] 'Spoken' discourse on SB could take a variety of forms, such as formal interviews, academic lectures, focus group discussions, and a recorded conversation on YouTube.

study's scope was limited to the Alberta context, it was, thus, considered important to pinpoint which of the discipline's envisioned product(s) would be of particular relevance to that province. To accomplish this, a product 'filtering' process (described as follows) was developed to identify an Alberta-product(s) for further analysis.

As informed by the research of others, four elements were considered relevant factors to consider when attempting to identify a product(s) of particular relevance to Alberta (see Figure 3.3). In sub-sections 3.3.1-3.3.3, as follows, the rationale behind the consideration of each element is discussed.

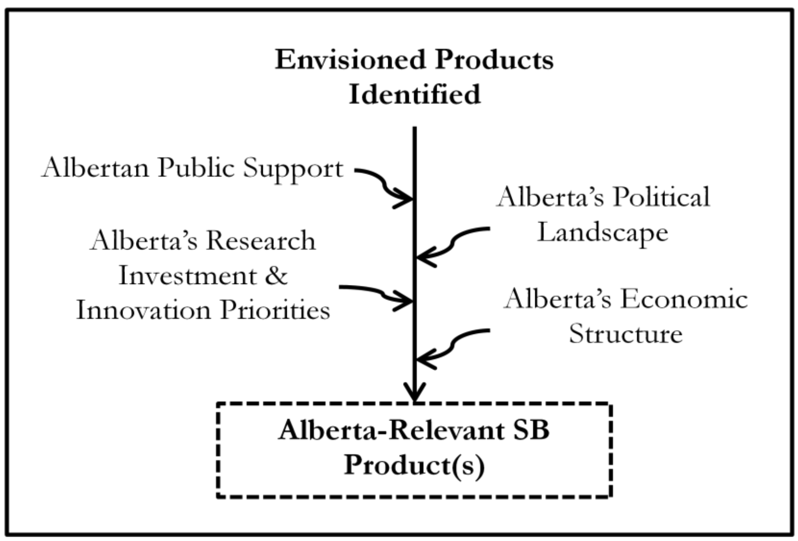

FIGURE 3. 3 THE CONCEPTUAL BASIS OF IDENTIFYING AN ALBERTA-RELEVANT SB PRODUCT(S)

3.3.1 PUBLIC SUPPORT

In democratic societies, public opinion/perception can be a "critical determinant" (137) of an emerging technology's acceptance or rejection (137)[10]. Within the context of SB some (138,139) have noted that, without public support for SB, both "funding and regulation

[10] Various factors may influence how people perceive science and technology, such as religious beliefs, cultural norms and values, as well as race (525). Generally, however, most people are supportive of science and technology (526)- especially of those that have the potential to benefit a wide range of people (204,233), and carry low safety concerns (230).

are unlikely to support significant scientific advances" (138) within the field. Indeed, as representatives of public democracies, governments might choose to fund research that promotes the development of SB products toward which public perception is positive. Conversely, they might also avoid funding the development of SB products that carry widespread negative public perception (140). As such, Albertans' opinion of an emerging SB product could play a substantial role in either promoting or hampering its commercial introduction and, ultimately, its adoption (141).

3.3.2 Political landscape and economic structure

As noted by Soetaert & Vandamme (142), an area's political landscape can influence whether a technology succeeds in an area. Indeed, if government policy initiatives are generally supportive of a particular technology, it is more likely to succeed over those that do not carry favourable political support. Along the same lines, Barrios (143) noted that innovations are normally successful when they are intricately linked to an area's economic structure. Certainly, if a technology has the potential to generate major financial returns for an area, it is more likely to be pursued than those unlikely to generate financial success (144).

3.3.3 Research investment and innovation priorities

Innovation has become an integral part of Alberta's overall economic diversification strategy (145). To help make the province an attractive world-class center of innovation, the Alberta Innovates organization was created in January 2010 as one part of the province's 'Alberta Research and Innovation Act' (146-148). This organization evolved from the reorganization of ten provincially-funded research and innovation organizations into four new corporations: Alberta Innovates- *Technology Futures, Health Solutions, Bio Solutions, and Energy &*

Environment Solutions as well as an advisory board: Alberta Innovates- *Alberta Research & Innovation Authority* (formerly, the Alberta Science and Research Authority) (149).

Of greatest interest to the province are research activities dedicated to supporting its largest economic sectors, including: energy, agriculture and agri-food, and forestry products (145). From a provincial standpoint, innovative technologies developed within these sectors would likely play a role in Alberta's future prosperity, and thus, would represent ideal areas for innovation (150). Toward this end, the Alberta Science and Research Authority reported four priority areas of focus for "science, research, technology, and innovation" (150) within the province, namely: 1) information and communications technology, 2) energy, 3) life sciences (health & wellness and agriculture/food/forestry and environment), and 4) nanotechnology (150).

3.3.4 STUDY ASSUMPTIONS AND CONCLUSIONS SURROUNDING THE SELECTION OF AN ALBERTA-RELEVANT PRODUCT(S)

Influenced by the information described in sub-sections 3.3.1- 3.3.3, several assumptions surrounding the identification of an Alberta-relevant product(s) were developed (Table 3.1).

TABLE 3. 1 ASSUMPTIONS SURROUNDING THE IDENTIFICATION OF AN ALBERTA RELEVANT PRODUCT(S)*

Category	Study Assumptions
Public Support	• An envisioned SB product would likely succeed in Alberta if: o it has the potential to benefit a wide number of Albertans, o carries low safety concerns, **and if** o Albertan public opinion/perception of the envisioned product(s) is generally positive
Economic Structure	• Envisioned products that could foreseeably complement Alberta's economic strengths would likely succeed in the province
Political Landscape	• Products that complement Alberta's political landscape would likely succeed
Research Investment and Innovation Priorities	• SB products that fall within the realm of Alberta's current and future areas of research priority (*e.g.* information and communication technology, energy, life sciences, and nanotechnology) would likely be explored by the province.

* These criteria were not weighted or ranked in terms of importance. All criteria were considered equally relevant for consideration.

By applying the previously described product identification process, this author assumed it possible to identify a range of envisioned Alberta-relevant SB products; each of which could then be categorized to fall within one of several application areas or sectors (*e.g.* health, energy, agriculture). Literature (130,151) suggests that envisioned SB products will likely require different forms of regulatory oversight, depending upon the sector in which they will someday be used. As such, it was considered both unwise and unfruitful to attempt to develop a single generalized statement about how *all* Alberta-relevant products might impact the lives of the province's citizens (75). This study, therefore, ultimately focused on the identification, and assessment, of only *one* of many possible Alberta-relevant products.

3.4 DIMENSION THREE: ADDRESSING THE CENTRAL RESEARCH QUESTION

To address the study's central research question (Figure 3.1, box C), its conceptual basis required further delineation. As a first step, it was necessary to *define the term* 'impact' and characterize its use within the context of the study (sub-section 3.4.1). The second step required the i*dentification of a process* that could be used to assess the potential impacts an envisioned SB product might someday have on the lives of Albertans (sub-section 3.4.2). In section 3.4.3, the conceptual basis of the central research question is summarized.

3.4.1 DEFINING 'IMPACT'

In this study, '*impact'* was considered in the plural sense and defined as the effects or influences (152) that an envisioned SB product might have on the lives of Albertans. In order to proceed further with the research, however, the term required further characterization, specifically, two questions first needed to be answered:

1) What *types* of impacts might these products have on the lives of Albertans?
and
2) Within what *context* could they be easily identified?

Numerous scholars have noted SB's potential to deliver enormous societal benefit. On the other hand, they also note the discipline presents society with a variety of risks (44-46,67,151,153). Based on this knowledge, this researcher made the assumption that the discipline's envisioned products could potentially impact the lives of Albertans in both positive and negative ways. Upon further reflection, this author determined that these two opposing impacts could be further characterized within the context of health. After combining these two concepts, a more refined version of the central research question evolved: *what benefits and risks might envisioned SB products have on the health of Albertans?*

As indicated by the literature, there are several ways to conceptualize health (4,14,154-156). As such, this element also required further characterization in order to proceed further with the study. Arguably, two of the most prominent lenses through which health is conceptualized include the biopsychosocial model of health and the contrasting biomedical model. In the section that follows, the meaning of these two conceptualizations is explored, and the rationale behind the one chosen for use in this study is articulated.

Defining 'Health'

According to the World Health Organization (WHO), health is "a state of complete physical, mental, and social well-being" (14). Inherent in this definition is the notion that a complex set of factors combine to influence the health status of both individuals and communities (14,154-156). These factors, commonly referred to as the 'determinants of health', can be broadly differentiated into three groups: a) the social and economic environment[11], b) the physical environment, and c) individual characteristics and behaviours (154,156). This 'biopsychosocial' perspective of health is contrasted by the biomedical perspective, which holds that good health is simply the absence of disease (4,5).

The biomedical model of health currently dominates in Western medicine (4,157). At its foundation also lies the concept of reductionism, meaning that every bodily malfunction- no matter how complex- can be explained in terms of a minimal number of biological factors (4,5). Indeed, only through physical intervention (*e.g.* medication or surgery) can the body be treated or cured of illness or disease (158). This model does not consider social and psychological factors in its definition of health. Instead, it assumes that the human body is an entity separate from the mind (4). As such, abnormal mind functioning must be explained by something physical and not social circumstance (5).

After closely reflecting upon each model of health, this author considered it inappropriate to approach the research question through a biomedical lens. Indeed, because most of SB's envisioned products remain in a conceptual stage, it would have been impossible

[11] According to the National Collaborating Centres for Public Health (27), 'social determinants of health' are a subset of determinants that focus on the "economic and social conditions that govern people's lives".

to identify, and quantify, an envisioned SB product's physical health impacts (45). This researcher recognized, however, that it was possible to identify the potential implications an envisioned SB product might have on Albertan's *social well-being*. This approach necessitated the adoption of a more holistic approach to the research, such as that described by the WHO's biopsychosocial model.

The decision to approach this research using a holistic perspective on health was also impacted by another important factor: the need to focus on 'Albertans' collectively, as a population, and not individuals (18). Certainly, good population health is a result of multiple determinants interacting together (14,155). Whereas the biomedical model is *individualistic* by nature and gives little attention to the social determinants of health, the biopsychosocial model of health is oriented toward groups of individuals or *populations*. It recognizes the wide range of complex conditions and factors that interact to contribute to the health status of populations (155).

3.4.2 Identifying the potential 'impacts' of an envisioned SB product(s)

The policy-oriented research practice referred to as 'technology assessment' (TA) provided the conceptual basis for addressing the study's central research question. The present sub-section addresses this topic by first exploring the concept of TA, and then moves on to explain the type of assessment best suited to address this study's central research question.

Technology Assessment

Technology Assessment (TA) is a process through which the possible short and long-term consequences of the application, and dissemination, of science and technology in society can be examined (159,160). As a scientific and communicative process, technology assessments aim to enhance societal understanding of the possible broad-reaching implications of science and technology (160). Ultimately, their goal is the production of knowledge and procedures to enable society to cope with the potential impacts of the items being assessed (161). As an important tool in the area of technology management, TA's can improve decision making on matters related to science and technology (159,160,162).

Various approaches to TA exist; however, the methods used to carry them out are largely dependent upon the current stage of development (or diffusion) of the items they assess (161-163). Broadly speaking, therefore, TA's can either be undertaken retroactively/reactively or proactively (162,163). For example, 'classical' or 'traditional' TA's are generally reactive, *i.e.*, they are undertaken in the later stages of an item's development when their "societal impacts can be easily identified and determined" (161)[12]. These types of assessments are largely data-driven, and often produce quantitative evaluations of an item's benefits compared to its risks.

Proactive technology assessments, such as upstream assessments (45,54) and horizon scans (164,165), are performed during the very early stage of an item's development. As such, they are necessarily speculative and require researchers to look forward in time to make predictions about the *possible implications* an item might bring to society (161,166)[13]. These types of assessments commonly involve the investigation and interpretation of data that are not as easily reduced to numbers.

Generally, classical technology assessments are quantitatively oriented, *i.e.*, the 'evidence' they produce aligns well with the positivist research paradigm that currently dominates within biomedical model of health (4). As such, these types of assessments have

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[12] Note that retroactive TA's can also be performed on a technology that is already disseminated (163).

[13] Guston & Sarewitz (170) advocate for 'real-time' TA, *i.e.*, ensuring that social science and policy research is integrated into science and technology research from its onset.

produced information traditionally considered more useful or reliable than qualitative research (167). Increasing calls to investigate the broader societal implications of technology at earlier stages of development, however, have begun to challenge this view. Indeed, many experts now claim that the findings of qualitatively-oriented technology assessments (*e.g.* some types of upstream TA's) can be just as valuable to decision makers (54,153,161,165,167).

'Upstream' Product Assessment

Currently, SB is in a nascent stage of development (106,153,168,169). As such, most of its products remain either in the early stages of development or simply visions of possibilities to come. Based on this knowledge, a *proactive* approach to technology (or in this case, product) assessment was required to address the study's central research question. As an important first step in the "anticipatory governance" (170) of SB, the information produced from such an assessment could help guide the responsible introduction of the discipline's future products into society (153,161).

3.4.3 SUMMARIZING THE CONCEPTUAL BASIS OF THE CENTRAL RESEARCH QUESTION

On the page that follows, Figure 3.4 illustrates the conceptual basis of the central research question.

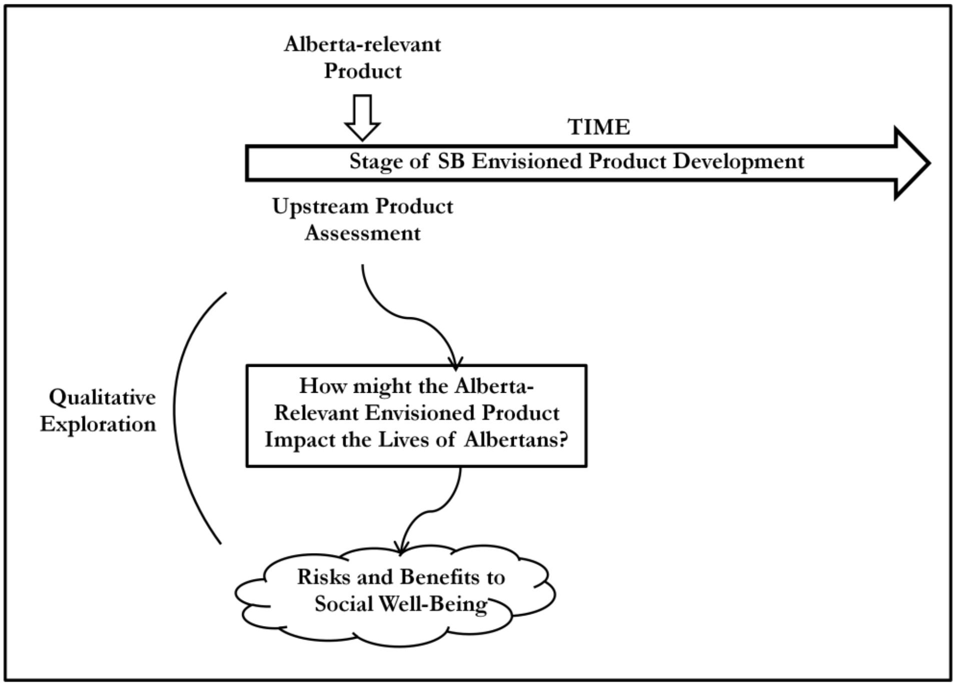

FIGURE 3. 4 THE CONCEPTUAL BASIS OF THE CENTRAL RESEARCH QUESTION

Briefly, this study was conducted under the assumption that the study's central research question could be addressed by conducting an upstream assessment of an Alberta- relevant product. To align with the study's purpose, this process has been termed an 'upstream product assessment'. Further, through the collection, analysis, and interpretation of qualitative data, this author expected the process to identify several risks and benefits related to the emergence of an Alberta-relevant product on the social well-being of its citizens.

3.5 FINAL CONCEPTUAL FRAMEWORK

Figure 3.5 (following page) presents this study's *final* conceptual framework, which was comprised of three interlinked, and elaborate, dimensions. The framework's **first** dimension involves the identification of envisioned SB products by scoping the content of relevant discourse. The framework's **second** dimension involves undertaking a product filtering process as a means through which to identify an Alberta-relevant SB product. The framework's **third** and final dimension addresses the study's central research question.

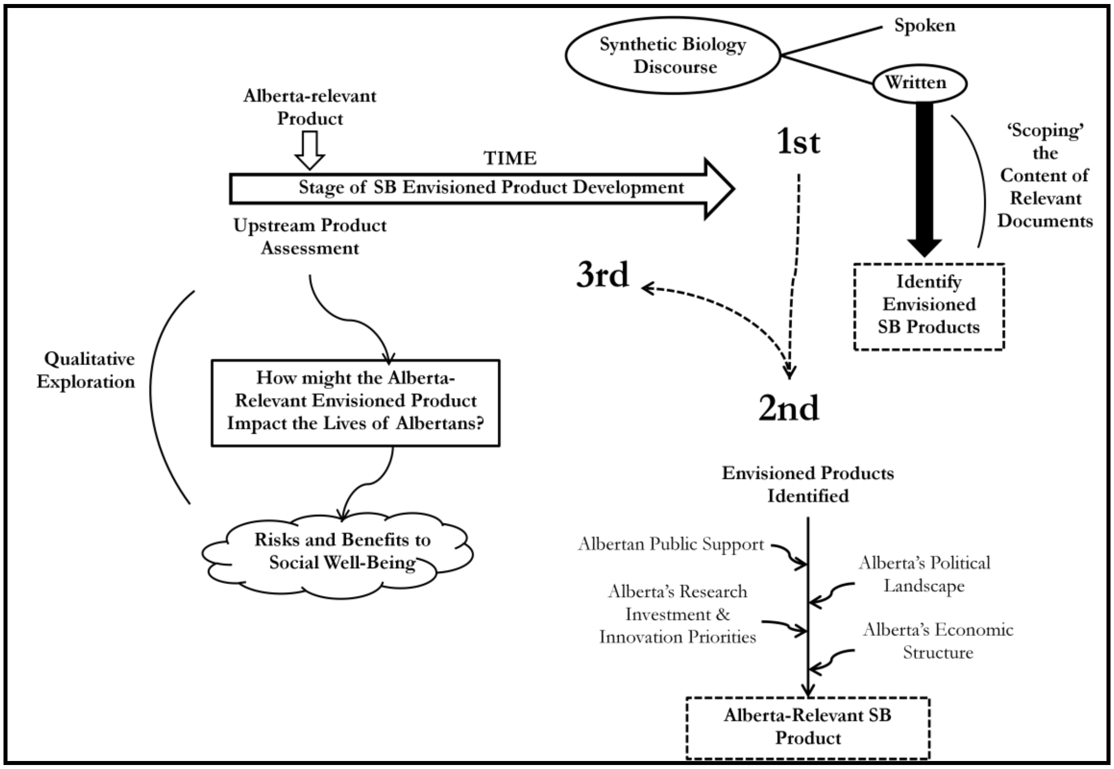

FIGURE 3. 5 A CONCEPT MAP ILLUSTRATING THE STUDY'S FINAL CONCEPTUAL FRAMEWORK

Now that the study's final conceptual framework has been established, this chapter continues with an explanation of the study's philosophical underpinnings, followed by a declaration of this researcher's perspectives on the study topic.

3.6 PHILOSOPHICAL UNDERPINNINGS OF THE RESEARCH

This qualitative research study is rooted in an interpretive or 'naturalistic' form of research inquiry (171). Its aim was to interpret meaning from the content contained within written discourse and to provide a broad, yet condensed, description of the findings. In contrast with more 'theoretically founded' qualitative studies (*e.g.* Grounded Theory), descriptive studies such as this produce a basic description of the data and are not highly interpretive. For example, researchers do not choose a specific conceptual, philosophical, or highly abstract framework or system through which to describe events (171).

In this study, language was considered a vehicle of communication, as opposed to a phenomenon that required interpretive assessment (171). As such, data interpretation remained closer to the surface of words and the study's findings have been provided in "everyday language" (171). While qualitative description is generally considered the least interpretive of all qualitative studies, it is more interpretive than quantitative description. Indeed, the data in this study was interpreted on the bases of pre-conceived expectations, assumptions, and variables (171).

3.7 Researcher's Perspectives on the Study Topic

Across all forms of qualitative inquiry, the researcher serves as the main instrument for data collection, analysis, and interpretation (172). Qualitative researchers are so closely connected to the data, thus, their perspectives play an inevitable role in shaping their research. To help readers understand how the author's views might have influenced the study, it is considered good practice to declare personal values, opinions, and biographical experiences (inherent biases) (173). In an effort to adhere to good practice, this author sought to identify personal biases that might have influenced the analysis and interpretation of data in this study. What follows is a brief description of this period of reflection.

Having obtained two previous degrees in science, this author approached the research with a positive perspective on scientific and technological innovation. Having identified this as potential bias, a conscious effort was made to maintain a centered opinion on the information encountered during the research process. Further, having **a)** conducted previous research in the field of climate change and **b)** worked in the area of bio-remediation, this author considered herself somewhat of an environmental advocate. Having recognized the possibility of becoming especially sensitive to information within this context, a conscious effort was made to keep this potential bias in mind throughout the research process.

3.8 Chapter Summary

This chapter outlined the basis of thought, and courses of action, taken to address the study's central research question (174). It played a key role in structuring the study's scoping review, which will be explored in the following chapter.

CHAPTER 4: SCOPING LITERATURE REVIEW

The previous chapter presented the study's conceptual framework. The present chapter summarizes the findings of a scoping literature review that was implemented to further guide the research process.

4.1 INTRODUCTION AND CHAPTER OUTLINE

This study was interested in understanding how an Alberta-relevant envisioned SB product might impact the social well-being of that province's citizens. To gain a deeper understanding of key literature published on matters related to this topic, a scoping review was carried out.

This chapter is structured as follows: first, section 4.2 provides a brief introduction to scoping review methodology. This is followed by a description of the search and selection strategy that was used to identify relevant literature (sub-section 4.2.1), and an outline of the methods used to chart (extract) pertinent information from that literature (sub-section 4.2.2). In section 4.3, the findings of the scoping process are summarized. The chapter then concludes with section 4.4, which provides a brief discussion of the research gaps identified and an introduction to the following chapter.

4.2 THE SCOPING REVIEW

A 'scoping exercise' or review is a relatively new type of policy-directed literature review employed to systematically assess the nature and range of discourse around a particular topic of interest (175). For many policy-relevant issues, such as the one addressed in this thesis, the time and rigorous standards adopted by traditional systematic literature reviews can be unsuited to the short window of decision-making available to many policy makers (176). Unlike traditional literature reviews, known for their in-depth analysis of literature and assessment of the quality of information reviewed, the goal of a scoping review is to "produce a profile of the existing literature in a topic area, creating a rich database of literature that can serve as a foundation for more detailed reviews" (177) [14].

4.2.1 LITERATURE SEARCH AND SELECTION STRATEGY

This scoping exercise was carried out based on the York methodology outlined by Arksey & O'Malley (133), and aimed to identify key sources of information published on three, targeted, topic areas:

1) 'Scoping' or surveying SB *product visions*,
2) Identifying SB *products* of relevance to Alberta, and
3) Assessing the potential impacts the discipline's *envisioned products* might have on a population using a 'proactive' assessment process.

To access relevant literature on these topics, this author searched for relevant literature across a broad spectrum of research areas from the biomedical sciences to social sciences and humanities as well as communication studies. Ultimately, relevant information was synthesized from two main sources: **grey literature** (reports published by non-governmental and governmental organizations as well as academic dissertations) and **peer reviewed research** (journal articles). Pertinent information retrieved from credible[15] **websites** was also collected. In this chapter, these three types of literature are collectively referred to as 'documents'.

[14] Arksey & O'Malley's scoping review methodology was also used to address one of the study's research questions (see section 5.2).

[15] Websites were deemed 'credible' if they originated from an academic organization, an academic research group, or a governmental or a non-governmental organization.

Databases and Keyword Search Constructs

Relevant documents were identified by conducting a series of literature searches via eight scientific literature databases, three theses and dissertation databases, and two Internet search engines (Table 4.1).

TABLE 4. 1 DATABASES SEARCHED IN THE SCOPING REVIEW

Scientific Literature	Theses & Dissertations	Internet Search Engines
• ISI Web of Science • BIOSIS Previews • Sociological Abstracts • Ovid Medline • Global Health • Annual Reviews • EMBASE: Excerpta Medica • ProQuest Interdisciplinary Research	• Theses Canada Portal • World Cat • Index to Theses (ASLIB)- From British and Irish Universities	• Google • Google Scholar

Each of the databases was searched for potentially relevant information using a combination of topic-specific keyword searches (Table 4.2), over a period of three weeks.

TABLE 4. 2 TOPIC-SPECIFIC KEYWORD SEARCH CONSTRUCTS USED TO SEARCH FOR RELEVANT CONTENT WITHIN THIRTEEN ELECTRONIC DATABASES*

Topic Area	Search Construct
Scoping or surveying SB's product visions	"synthetic biology" **OR** "synthetic genomics" **AND** scope, scoping, review, discourse, communication, content analysis
SB products of relevance to Alberta	"synthetic biology" **OR** "synthetic genomics" **AND** Alberta **AND** political landscape, politics, economic, economy, innovation, support, opinion
Assessing potential impacts of SB's envisioned products (within the context of social well-being)	"synthetic biology" **OR** "synthetic genomics" **AND** assessment, analysis, governance, policy, framework, well-being, wellbeing, social, health, holistic, social determinant, impact, evaluation, evaluate, foresight

* Subsequent literature searches were performed to gain further insight on key topics (*e.g.* proactive or upstream technology assessment and the precautionary principle) uncovered during these searches using similar processes described throughout this section.

Inclusion Criteria

Documents retrieved from database searches were considered potentially relevant if they were: a) published in the English-language from b) the year 2000 to the search date (inclusive) and c) classified as one of three types of documents described in section 4.2.1. After scanning for inclusion against these three criteria, documents were then scanned for relevance based on their content. Specifically, only documents that:

1) discussed, or performed, a quantitative survey of SB's product visions over time, and/or a qualitative analysis of envisioned SB product discourse, or
2) discussed what types of envisioned SB products might be of particular relevance to the Province of Alberta or provided insight into i) Albertan public opinion on SB products, ii) the province's research/innovation priorities, iii) its political or iv) economic landscape, or
3) identified potential impacts that an envisioned SB product(s) might someday have on the social well-being of a population, or discussed elements that should be included if such an assessment were undertaken

were eligible for review. Grey and peer reviewed literature were scanned for content relevance first by title, then by abstract or report summary, followed by full text. Websites were scanned for relevance first by search hit i) title, then by ii) short summary, followed by iii) full webpage content.

4.2.2 Charting Relevant Data

Relevant information from each of the selected documents was synthesized and interpreted by scanning, charting, and sorting relevant material according to similar themes. For research studies, information was recorded on study aims, methodology, and important/relevant results.

4.3 Findings

During the literature scanning process, this author identified, organized, and categorized pertinent information into themes until the point at which no new information was obtained. Ultimately, these procedures enabled key information to be assembled on the four topics of interest. In the sub-sections that follow (4.3.1 to 4.3.4, inclusive), the findings associated with each of those topic areas of interest are described.

4.3.1 Scoping or surveying SB's product visions

This scoping exercise identified several previously published research and grey documents that either 1) discussed broad application areas wherein SB as discipline might someday become important (*e.g.* in the area of human medicine) or 2) presented simple examples of specific products that might someday become realized (*e.g.* cancer scavenging microbes). No studies located, however, scoped the literature in an effort to systematically identify and map the breadth of SB product visions made over time[16].

A total of n=32 academic review articles identified during this scoping review surveyed the current state of SB research within the context of broad-reaching *application areas*. For example, most articles (41%) retrieved discussed current research progress in energy-related applications of SB (178-187). Others reviewed the discipline's potential to influence the area of human medicine (132,188,189), while others, still, focused their discussion on the discipline's potential to positively impact the area of industrial chemistry (190-192) and the environment (193-195). At least three review articles identified discussed specific SB product visions, but the authors presented only simple examples of products that might someday become realized within a small number of application areas (132,196,197).

In addition to the review articles discussed above, this author retrieved numerous other *single study* journal articles that listed examples of envisioned SB products that might someday come into fruition. Indeed, other articles revealed that, whether or not an important or valid undertaking, it was beyond their studies' scope to identify 1) the wide range of potential products SB might someday produce or 2) the application areas wherein SB as discipline might someday become important (198-202). In the end, no journal articles retrieved identified and mapped the breadth of SB product visions made over time.

In contrast to scientific literature, relevant reports retrieved from this scoping exercise appeared particularly engaged in discussion on the discipline's potential products. For example, a May 2009 report published by the Royal Academy of Engineering devoted an entire chapter

[16] The United Kingdom Executive's Biological Agents Unit expressed interest in undertaking a scoping exercise to identify a collection of SB applications that might be of relevance to Great Britain (527). As of this study's publication date, however, this exercise has not been undertaken.

(three) to envisioned SB products, and placed particular emphasis on the potential economic benefits they might someday bring to society (108). Further, this report discussed five major 'application areas' of the discipline, and provided examples of specific product visions that fit within those areas, such as biological sensors (108). An additional two 'Concept Note' reports published by the International Risk Governance Council (IRGC) each discussed a selection of 'likely' SB products that might emerge in three main application areas: environment, health, and industry (130,131). Further, a 2009 American-based report identified during this literature scoping exercise (203) also devoted a sizable portion of discussion to specific examples of envisioned SB products that might someday emerge in society (203).

At first consideration, the grey literature described above appeared to identify and map a wide range of SB product visions over time. Upon closer reflection, most reports provided neither the search strategy used to identify the products discussed, nor explicit references for the product information they presented (52,108,130). Indeed, in the end, these reports were not systematic in their efforts to identify and map the breadth of product visions they discussed. As such, while the product predictions made by the reports could in fact be completely valid, this researcher calls the completeness of the information they presented into question. Clearly, a knowledge gap within this domain currently still exists.

In addition to the information described previously, the scoping exercise also identified studies that examined the *nature of discourse* surrounding SB and its product visions. These findings are briefly explored in the discussion that follows.

Grant & Williams (204) emphasized the importance of investigating and evaluating the nature of dialogue around SB, maintaining such endeavours would allow policy to become focused or 'framed' by a variety of interests and a range of perspectives. They asserted such activities would allow for improved decision making on SB and would help increase the likelihood that the discipline's emerging products would someday benefit a wide range of people. Pauwels (205) also emphasized the importance of analyzing the nature of discourse surrounding SB. The findings of this focus group study revealed the manner in which SB's potential applications were presented or 'framed' by the group leader influenced the way the discipline was, in turn, perceived by participants.

The nature of SB discourse was also examined in a 2008 report by Pauwels & Ifrim (105). In this study, the authors examined a variety of aspects relating to the nature of SB discourse found in American and European newspapers. Briefly, these authors found marked differences in the frequencies with which certain envisioned SB products were discussed in European newspapers, compared to those based in America. For example, European press mentioned the SB energy and environmental products more frequently than health-related products. Conversely, the American press mentioned SB's health related products more frequently than environmental products. The authors attributed those differences to geographical priorities. Indeed, the media might have biased their coverage of envisioned SB products toward those of greater priority or interest to their geographical area.

Cserer & Seiringer (206) also examined the nature of SB discourse in news media by employing content analysis on German-language newspapers. These authors aimed to answer a variety of questions, such as: how SB was represented by the German-language news media articles they analyzed. Their findings showed that, at least in German-language media, the majority of products and applications discussed centered on bio-remediation and the creation of bio-fuels (206).

4.3.2 IDENTIFYING SYNTHETIC BIOLOGY PRODUCTS OF RELEVANCE TO ALBERTA

This scoping review used two main approaches to help identify what SB products might be of greatest relevance to the Province of Alberta. **First**, the literature was surveyed for information about Alberta's current and historical SB research landscape. **Second**, as influenced by the study's conceptual framework, the literature was scanned to locate information pertaining to the four elements described in Figure 3.3, which included: 1) Albertans' public opinion toward SB products, as well as the province's 2) political landscape and 3) economic structure, and its 4) research and investment priorities. This author hoped that, when taken together, this information could be used to identify an Alberta- relevant SB product. Once one product was identified, its potential impacts on the social well-being of Albertans would be assessed.

Alberta's Synthetic Biology Research Landscape

Alberta Ingenuity (now part of Alberta Innovates- Technology Futures) has described the Province of Alberta as a "leader in synthetic biology", claiming the discipline has the potential to "create a foundation for a robust, knowledge based [Albertan] bio-economy" (207). Perhaps not surprisingly, this organization has offered financial support and educational resources to the province's iGEM teams since 2006 (208). As described in chapter two, because iGEM is the premiere undergraduate competition in SB, this author considered the province's level of iGEM involvement as relative indicator of its overall interest in the discipline (116).

Alberta iGEM teams

A scan of relevant literature revealed the Province of Alberta has increased its presence at the iGEM competition since 2006. Among Canadian iGEM teams, Alberta has been especially prominent. As illustrated in Figure 4.1., in 2007 and 2008, approximately half (50 and 58%, respectively) of all Canadian iGEM teams were from Alberta.

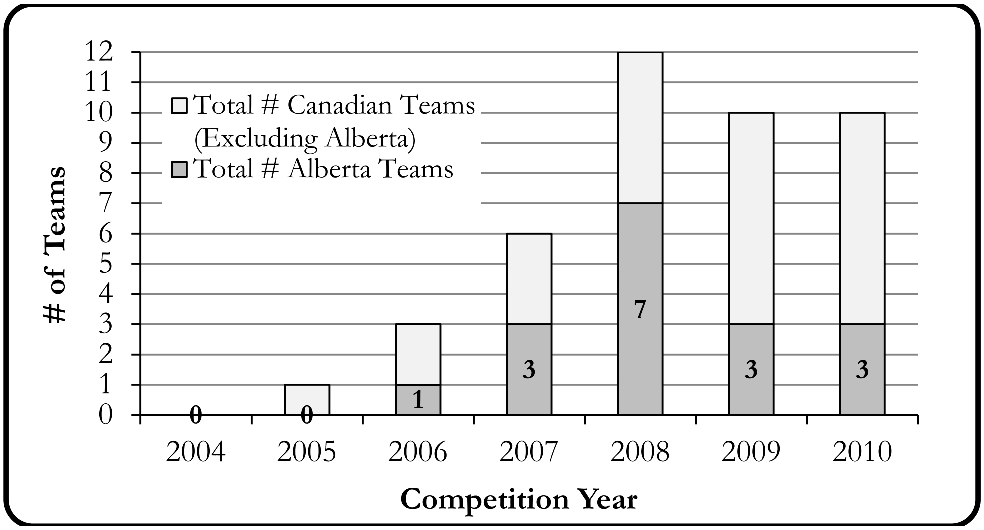

FIGURE 4. 1 NUMBER OF CANADIAN AND ALBERTAN IGEM TEAMS IN 2004-2010

Perhaps the most well-known Alberta-based iGEM team originated from the University of Alberta in 2007. This team, referred to as the 'Butanerds', won first place in the competition's Energy and Environment category for their creation of modified *E.coli*, capable of producing bio-butanol transportation fuel (108). This team also received international media attention for their work when their organism was named to Wired Magazine's top 10 list of new organisms for 2007 (209). This win was the impetus for the creation of the first course in SB at the University of Alberta in 2008. It was primarily designed to help more Alberta teams succeed at future iGEM competitions (210).

The 'Butanerds' research continues to be pursued at the University of Alberta's Bio-refining Conversions Network (211). Currently, however, the Network's researchers are engineering *yeast*, not *E.coli,* to ferment provincially-grown sources of biomass and produce bio-butanol (212,213). Indeed, whereas the Butanerds provided proof of principle for the technique, researchers at the Bio-refining Conversions Network are working to overcome two common problems of microbial-based bio-fuel production: bio-fuel toxicity (product causes harm to the organism that produces it) and low product yield (213).

'Other' Alberta-based synthetic biology research

Apart from bio-fuels research, Alberta also plays host to other important SB research, such as the 'PhytoMetaSyn' project. This project, currently being led by Dr. Peter Facchini of the University of Calgary and Dr. Vincent Martin of Concordia University, uses SB techniques to identify important genes from more than 70 plants that could be used to produce a variety of important chemicals (*e.g.* pharmaceuticals, flavours) (214). In essence, the researchers aim to create a catalogue of important plant DNA 'parts', reminiscent of the Registry of Standard Biological Parts (215). As another key part of the project's deliverables, other team members are currently performing "an analysis of socio-economic, environmental, legal, and ethical impacts" related to SB (214).

Public Opinion, Research and Innovation Priorities, Political and Economic Landscape

The previous sections discussed the province's overall SB research landscape. In the sections that follow, Albertans' public opinion on the discipline's envisioned products, the province's research investment and innovation priorities, political landscape and economic structure are discussed.

Albertans' public opinion on synthetic biology

No published academic or grey literature discussing Albertans' opinion on envisioned SB products was identified. A simple Google search, however, identified preliminary, unpublished, results from a series of 2010 Canadian public opinion surveys on SB issued by the PhytoMetaSyn research group (214). One survey, which aimed to identify Albertan public opinion on the discipline, revealed that the majority of Albertans surveyed were supportive of using SB in bio-fuel and medical applications. In contrast, the notion that SB could someday be used in bio-remediation and for military application generally caused concern for those surveyed (216). Another article, published by Priest (217), offered complementary insight on this matter. It revealed that, in general, Albertans tend to be supportive of most emerging technologies.

Given the information above, it is perhaps not surprising that 'innovation' has become an integral focus of the province's efforts to diversify its economic activity (145). Indeed, the provincial government devotes nearly $200 million annually to research activities that are mainly dedicated to supporting its largest economic sectors: energy, agriculture, and forestry (145). In the discussion that follows, the province's research and innovation priorities are explored in further detail.

Alberta's research and innovation priorities

As previously discussed (see sub-section 3.3.3), in January 2010, the Alberta Innovates organization emerged from the integration of ten previously established Alberta-funded research and innovation organizations in hopes that it would become a "catalyst of innovation" (146) for the province. Along with Alberta's technological commercialization action plan, Alberta Innovates- Alberta Research & Innovation Authority (advisory board) and the four networking agencies it oversees: **1)** Energy & Environment Solutions, **2)** Bio Solutions, **3)** Health Solutions, and **4)** Technology Futures have been designed to help make the province an attractive world-class center of innovation (147,218). Given their potential relevance to SB, these four agencies will be described in further detail directly in the paragraphs that follow.

Alberta Innovates- Energy and Environment Solutions

To help ensure that Alberta remains a global leader in energy-based hydrocarbon research and technology, Energy and Environment Solutions was created to pursue novel research in energy exploration with special focus on what the agency terms "ecologically responsible energy" and renewable energy technologies (146). Currently, through collaborative efforts with other research institutes, this agency is developing the "next wave of [renewable energy] solutions", including waste-to-biofuel technology (146). This agency's goal is to use these solutions to help enhance the environmental, economic, and social well-being of Albertans and populations beyond (146).

Alberta Innovates- Bio Solutions

Bio Solutions aims to support the development of novel technologies for the global bio-economy. This agency aims to build on the strengths and successes of four other Alberta-based research institutes, including the Alberta Prion Research Institute, the former Agricultural Research Institute, the Alberta Forestry Research Institute, and the Alberta Life Sciences Institute (146). Currently, Bio-Solutions' research focus lies in bio-refining, composite materials, food and health products with value-added properties, and nanoscale technology (146).

Alberta Innovates- Health Solutions

Through improved collaborations between research and technology development initiatives, Health Solutions aims to stimulate and continue to guide pioneering discoveries, novel tools, process, technologies, and an increased understanding of health and disease. This agency hopes that these initiatives will someday improve the physical health and social well-being of Albertans and of populations in the world beyond (146). With Alberta's strong natural resource-based economy, the province has become especially invested in environment and community health research, calling it a 'strategic priority' for the province (147).

Alberta Innovates- Technology Futures

Technology Futures builds on the mandates and successes of four previously-established Alberta research and development organizations, namely: Alberta Ingenuity, the Alberta Research Council, iCORE, and nanoAlberta. This agency offers technical services, funding, and commercialization support to entrepreneurs, corporations, researchers and investors in an effort to create healthy and sustainable Alberta businesses. In addition to helping build globally competitive Alberta-based commerce, the agency aims to prepare the province for a "next generation economy" (219).

Now that the province's research and innovation priorities have been explored, this chapter continues by outlining Alberta's economic landscape.

Alberta's economic landscape

Thanks to a major Alberta oil discovery in 1947, which initiated a series of numerous other oil and gas discoveries across the province, Alberta has become the hydrocarbon-based energy centre of Canada (220,221). There are three main types of fossil fuel-based resources in Alberta, including oil (conventional and oil sands), natural gas, and coal (145). The government currently invests approximately $30 million CDN every year in research related activities within this domain to ensure the industry remains strong and active.

Owing to the success of the province's booming energy industry, of which the 2008-2009 oil sands royalties alone generated $3 billion for the province, Alberta's Per Capita Gross Domestic Product ranks first in the nation at $ 50 986. This value is approximately $ 11 000 more than the Canadian national average and almost 25% higher than the second ranked Ontario (145,221,222).

Aside from the energy sector, agriculture and forestry also provide important contributions to Alberta's thriving economy. Indeed, Alberta has one of the most productive agricultural economies in the world with 20 million hectares of land devoted to the production of livestock and crops (223). The province is the nation's second largest producer of agricultural products with beef, wheat, canola, and pork representing its four most valuable agricultural commodities (224). In 2005, Alberta's field crops (wheat, oats, barley, canola, and dry peas) represented more than one third of the nation's entire production (145).

As Alberta's third biggest economic division, the forest product industry generates in excess of $11 billion a year for the province (225). With 60 percent of the province covered in forest (the Green Area), translating to 38 million hectares, the industry employs between 38-44 thousand Albertans in primary and secondary forest-related product manufacturing (145,225). Due to the rising Canadian dollar, and a dramatic decrease in the North American housing industry, Alberta forestry has fallen into a deep economic slump over the past year that is the worst the industry has seen in the past three decades (225).

Alberta's political landscape

For nearly eight decades, Alberta's government has remained conservative and "staunchly pro-business" (226). While this market-driven conservative attitude has contributed to Alberta's economic growth and prosperity, the source of its wealth has also received a great deal of criticism from environmental groups (220).

In 2010, the Corporate Ethics International launched their 'Rethink Alberta' anti-tourism campaign , which gained widespread media coverage in protest to the expansion of the

Alberta oil (tar) sands, referring to them as the "other oil disaster" (227). On their website, the organization urged the public against visiting the province until the government of Alberta adhered to two main conditions: stopping the oil sands expansion, and taking significant steps toward incorporating cleaner energy sources as a foundation of their economy (227).

In response to the immense environmental criticism described above, the province has begun investing in the development of renewable bio-fuels, which it claims will stimulate the province's bio-based economy (228,229). Indeed, the province has chosen to adopt the federal government's $1.5 billion biofuels initiative, which it has dubbed the 'Renewable Fuels Standard'. This standard requires that at least five percent of gasoline used in 2010 be composed of renewable fuels and that approximately two percent of diesel fuel and heating oil be composed of renewable fuels by 2012 (229,230).

The previous sections highlighted key sources of information intended to provide this study with further guidance on choosing an envisioned SB product of relevance to the Province of Alberta. In the following sub-section, the results of a scan for SB literature on performing a predictive or upstream assessment of the discipline's product visions are discussed.

4.3.3 ASSESSING POTENTIAL IMPACTS OF ENVISIONED SB PRODUCTS

Synthetic biology presents a unique challenge to decision makers: its true impacts on society cannot yet be fully conceptualized because most of the discipline's products do not yet exist. Yet, as shown in Table 4.3, this scoping review identified several studies that emphasized an urgent need to investigate, assess, and address, the potential impacts SB could have on society- *before* its products become widely developed and commercialized.

TABLE 4. 3 STUDIES EMPHASIZING THE NEED FOR PROACTIVE ASSESSMENT/ACTION IN THE FIELD OF SB

Study	Type of Proactive Assessment/Action Needed	Rationale
Balmer A, Martin P. (2008) (139)	Anticipatory intervention; a robust governance framework must be in place before SB's applications are realised	It is too late to wait to assess the potential impacts of a technology until issues arise through its practical application
No author cited (Governance report) (2008) (231)	Social, ethical, and safety considerations need to be made early in the life cycle of SB research, its development, potential applications, testing, and final use	Many scientists support a move to define the social and ethical issues of emerging technologies before they reach the point of impact.
Kuzma J, Tanji T. (2010) (54)	Look "upstream" to anticipate SB's possible social impacts prior to wide-scale deployment and use.	Many emerging technologies have brought the world unanticipated negative impacts that might have been prevented if their societal risks were assessed early enough.
T. M. Tanji. (2009) (45)	Look "upstream" to anticipate SB's possible social impacts prior to wide-scale deployment and use.	Addresses the need for public engagement; helps ensure that societal values are upheld throughout SB's development. It can also help ensure that a level of transparency is upheld during the development of relevant oversight frameworks.
Lowrie H, Tait J. (2009) (131)	Policymakers and regulators should try to shape, rather than respond to, SB's scientific developments	In other areas of life sciences (*e.g.* genetically modified crops), early policy decisions on appropriate regulatory precedents have been the key to their evolution
Lentzos F. (2009) (232)	Ethical and social issues should be identified at an early stage in SB's development- before new products/processes emerge	Research funders and researchers need to be able to consider this type of information to help make informed decisions
Preface of: *Parens E, Johnston J, Moses J.*(2009) (233)	A number of ethical issues should be addressed early and proactively	Too often, ethical concerns are addressed after technologies are mature and marketed. At that point, there is little incentive to address these issues because any debate may smother innovation and advancement **(Cont'd)**

TABLE 4. 3 (CONT'D) STUDIES EMPHASIZING THE NEED FOR PROACTIVE ASSESSMENT/ ACTION IN THE FIELD OF SB

Study	Type of Proactive Assessment/Action Needed	Rationale
Schmidt M, Ganguli-Mitra A, Torgersen H, et.al. (2009) (234)	New methods of risk assessment	To decide whether a new SB technique or application is safe enough for use in the open environment.
Schmidt MR, Kelle A, Ganguli Mitra A.(2007) (235)	A foresighted technology assessment	Given former (negative) experience in the societal aspects of various biotechnologies
Tucker JB, Zilinskas RA. (2006) (43)	An early, wide- reaching, debate about how best to guide SB in a safe and socially useful direction	It is already too late to impose a moratorium on SB, but early assessment is still needed

As illustrated in Table 4.3, several in-depth reviews, original research studies, and research organizations have acknowledged the need to reflect upon the potential wide-reaching social implications related to SB as a discipline. Indeed, several others (52,87,104,108,130,139,151) have also performed various types of proactive assessments on *SB as a whole*, largely in an effort to help ensure that the discipline's potential benefits can be realized through responsible development. As stated at the outset of this thesis, however, this study was interested in understanding how an envisioned *SB product* of relevance to a particular geographical area might someday impact the lives of citizens that live within that area (see section 1.2). As explained in the paragraph that follows, across the literature examined, this author identified only one study (198) that addressed a similar goal.

In their 2009 study, Wellhausen & Mukunda (198) preformed what they termed a 'predictive analysis' on how SB's future application in the realm of synthetic chemical production might impact the (political) economy of developing countries. To illustrate their point, the authors drew upon information gained from two historical cases of natural chemicals that faced potential "market dislocations" (198) when synthetic competitors were realized: rubber in Malaysia and indigo dyes in India. While the context of their study was different, it did provide some initial insight on how a proactive assessment could be carried out on an envisioned SB product. In the end, however, its lack of methodological detail about how to achieve results left a knowledge gap that required further investigation on the part of this researcher.

To fill the knowledge gaps identified above, this author sought further guidance on how to conduct an upstream assessment of an envisioned SB product. First, additional information was identified, retrieved, and charted from SB literature. Next, relevant information from previously established assessment frameworks applied within the context of other emerging technologies was sought and collected. In the sections that follow, the findings that emerged from these searches are described.

The Key Elements of a Proactive Assessment of SB Products

A review of relevant literature uncovered six inter-linked categories of elements that some suggest should be considered when undertaking a proactive assessment of envisioned SB products and/or other novel genetic technologies. Table 4.4 (follows) illustrates these elements and describes the rationale for considering their incorporation within this study's SB product assessment.

TABLE 4. 4 SUGGESTED ELEMENTS TO CONSIDER WHEN UNDERTAKING A PROACTIVE ASSESSMENT OF ENVISIONED SB PRODUCTS AND RATIONALE THEREOF

Suggested Element	Rationale
Ethical implications (45,54,200,236-239)	• Although most ethical issues are related to social issues, not all social issues are ethical issues • Can help identify broader range of potential issues, such as the equitable distribution of the product(s)
Implications from the point of view of various stakeholders (54,130,131,231, 234,237)	• SB's envisioned products can sometimes present a unique set of social and ethical concerns to various stakeholders
ELSI and GE3LS: Ethical, environmental, economic, legal, and social implications (238,239)	• These frameworks can be used to examine the values underlying the use of novel genetic technology- prior to its actual use in society • Ethical, legal and social issues may be real or perceived, but this distinction often does not matter to consumers and policy makers
Implications associated with replacing conventionally used counterparts and methodological approaches with SB products and techniques (203,237)	• If a SB product is set to replace a conventionally used product, it should be at least as safe as the conventionally used product • Organisms created using SB should be just as safe as those created using conventional genetic engineering
Historical experiences (45,54)	• Can help researchers identify how SB's emerging products might someday impact society, including key oversight issues
Intellectual property, biosecurity, and biosafety issues related to the emergence of SB products (54)	• Issues raised over SB's intellectual property are never completely separate from biosafety, biosecurity and ethical matters and should be considered equally as important in the oversight assessment process

In the sections that follow, each of the six elements illustrated in Table 4.4 will be explored in further detail.

Ethical Considerations and Stakeholder Point of View

As illustrated in Table 4.4, several studies have noted the importance of identifying ethical implications associated with the emergence of SB products into society (45,54,200,236-239). As noted by Ebbesen *et.al.* (240), the "open-endedness" and dynamic nature of

Beauchamp and Childress' four Principles of biomedical ethics (241) makes them appropriate to guide the discussion and conceptualization of ethical issues in the emerging field of SB (242,243) (see Table 4.5). Indeed, these four Principles described have been used to perform ethical-based decision making in the field of bio-medicine for many years (240,244).

TABLE 4. 5 BEAUCHAMP AND CHILDRESS' PRINCIPLES OF BIOMEDICAL ETHICS

PRINCIPLE OF BENEFICENCE	**PRINCIPLE OF NONMALEFICENCE**
Doing what is best for others. Under this ethical principle, one ought to do and promote good, prevent and avoid evil and/or harm and "weigh and balance the possible goods against the possible harms of an action"	The principle of nonmaleficence compliments that of beneficence. This principle states that one ought to avoid causing intentional harm. More specifically one must not cause others physical or mental harm
PRINCIPLE OF RESPECT FOR AUTONOMY	**PRINCIPLE OF (DISTRIBUTIVE) JUSTICE**
Refers to those who are competent to make their own decisions. Those who are not are still protected by beneficence and nonmaleficence. Generally, this principle implies that one should not be coerced into making a decision and others are obligated to protect the confidentiality and privacy of others, and "fostering autonomous decision-making"	This principle refers to the fair distribution of resources, *i.e.,* everyone should have equal access to goods and services that "every rational person values" should not be a privilege of an individual, but a social good that ought to be distributed equally for all individuals.

In today's pluralistic society, various stakeholders affected by a particular issue hold different values that sometimes conflict with others. Indeed, various stakeholders will likely be impacted by emerging technologies in different ways and, as such, should be considered separately during impact assessment (130,131). As part of responsible democratic process, many studies emphasized the need for all SB stakeholders to be given an opportunity to voice their concerns about the discipline (30,104,231,232,234,245). Applying this view within the context of this study, this author assumed that SB's envisioned products would likely present a unique set of social and ethical concerns for various stakeholders (54,130,131,231,234,237). Indeed, the integration of stakeholder values can help reduce the potential that decision makers ignore the values of the weakest players. The notion that stakeholder views should be incorporated into ethical considerations is at the basis of applied ethics, which Mepham (246) drew upon in his creation of the 'Ethical Matrix'.

Mepham's Ethical Matrix was created to be used as a tool for analyzing the potential ethical impacts of an emerging technology. It is composed of two main elements: on the horizontal axis, the four Principles of Biomedical Ethics (Table 4.5) are categorized into three groups: well-being (a combination of beneficence and non-malfeasance), autonomy (or freedom), and justice. Mepham justified the combination of beneficence and non-malfeasance into a single Principle called 'Well-being' because it simplifies the framework and, for many proposed technologies not directly related to medicine, their individual importance is often not weakened by combining them (246). On the vertical axis, those who stand to be affected by a new technology (the stakeholders) are listed. Once the Matrix is created, the researcher identifies and documents the ethical impacts under consideration within each matrix cell (247).

ELSI and GE3LS Frameworks

This scoping review revealed two relevant social implication 'classification' frameworks, frequently used to identify social implications of emerging genetic technologies (238,239). These frameworks, which are best known by their acronyms, include: the World Health Organization's *ELSI* framework (238) and Genome Canada's framework *GE3LS* (239). ELSI stands for ethical, legal, and social implications, and GE3LS stands for genomics-related ethical, economic, environmental, legal, and social aspects. SB shares many of the same social and ethical concerns as other genetic research, thus, the elements defined within ELSI and GE3LS were considered potentially appropriate within the context of this study.

Replacing Conventionally used Counterparts and Methodological Approaches

Two studies (203,237) identified during this literature scoping exercise emphasized the need to consider the potential implications (risks and benefits) associated with:

a) replacing *conventionally* used counterparts with novel SB products (237)
and
b) organisms created using *conventional* genetic engineering techniques compared to those created using SB (203).

These two studies will be briefly explored in the paragraphs that follow.

In their 2009 report, Capurro *et al.* (237) emphasized that, in addition to evaluating the potential implications SB's potential products could have on Europeans, impact assessments should also consider the risks and benefits of replacing conventionally used technologies with those products. This author identified one recently published study that considered this issue within the context of SB (198). Briefly, in their 2009 study (mentioned previously), Wellhausen & Mukunda (198) explored the potential impacts of replacing two naturally-produced chemicals with SB-created chemical counterparts.

As the field of SB advances, practitioners might someday be able to produce an entirely novel organism from scratch. As noted by Rodemeyer (203), decision makers should consider whether novel organisms created using SB techniques present greater risks to society than organisms created using conventional genetic engineering techniques. Indeed, the novelty and potential power of SB *techniques* should be considered inherently more risky than conventional genetic engineering. The 'living' *products* the discipline's practitioners might someday create, however, might also pose novel or enhanced risks to society.

Historical Experiences

This author identified three studies (45,54,198) that drew upon history to make predictions about how SB's envisioned products might someday impact society, including potential oversight issues. In the discussion that follows, the 'historical' methods used in each of these studies are explored.

Wellhausen & Mukunda (198) preformed a predictive analysis in an effort to identify how SB's potential application in the chemical industry might impact the economy of developing countries. The authors drew upon information gained from two historical cases of natural chemicals that faced potential "market dislocations" (198) when synthetic competitors were realized: rubber in Malaysia and indigo dyes in India.

In his 2009 thesis published by the University of Minnesota, Tanji (45) drew upon two historical case studies: 1) the emergence of semiconductor technology and 2) "first generation biotechnology" (45), to help identify several oversight issues that might become particularly relevant SB. While the previously described Wellhausen & Mukunda study focused on one type of envisioned SB application area (chemical production), Tanji's thesis (45) drew upon a range of historical examples, which led to the identification of several oversight issues (*e.g.* informed consent, biological crimes, product negligence, intellectual property, and issues related to socio-economics), applicable to a wide-range of potential SB products.

In 2010, Tanji co-authored an article with Jennifer Kuzma (54)wherein key oversight policy issues for SB were also identified and discussed. Again, the authors identified key issues pertaining to SB oversight by drawing upon information gained from historical experiences. In this study, however, the authors primarily drew upon the historical emergence of biotechnology and nanotechnology.

4.3.4 THE IDENTIFICATION AND ASSESSMENT OF 'RISK'

Upon closer examination of the content identified in this scoping review; this author noted a particular emphasis on the need to identify the potential *risks* associated with SB's products, as opposed to both risks *and* benefits or just benefits. Indeed, at least five (45,54,130,131,237) studies identified discussed the need to develop a proactive approach to *risk assessment* in the field. This conceptualization of oversight within the context of SB is exemplified by the 'precautionary' principle. Given the prolific discussion surrounding this principle within the context of SB, this author felt it pertinent to discuss its relevance within the context of this study (as follows).

The Precautionary Principle

Since its origin in the 1970's, the precautionary principle has influenced a number of environmental and public health policies, including those concerning genetically modified organisms and global warming (10,248,249). At the foundation of this risk-oriented principle lies the notion that, when action is taken and/or policies implemented, the overall risk to the public and the environment must not increase (153,250). It recognizes that decisions are often made during times of uncertainty and there is no need for complete evidence of a risk before action can be taken to mitigate its potential effects (248). As such, it calls on decision makers to prevent or delay the emergence of a novel technology if there is a reasonable and logical risk of harm to the environment and/or public health (251).

The precautionary principle is particularly relevant during the risk management phase of the risk analysis[17] process (252,253). During this phase, decisions are made about whether assessed risks are sufficiently high to present a concern to public health and the environment.

[17] There are three inter-related phases of risk analysis: risk assessment, risk management, and risk communication (24)

Policy alternatives are weighed and appropriate prevention and control options are then selected (24,26). As a tool through which to identify the nature and magnitude of potential harm, risk assessment plays a vital role the risk management process (253). When undertaken through a precautionary lens, risk assessment calls for the identification and characterization of a broad range of potential harms (*e.g.* social, ethical, and economic) that a novel technology could bring society as early as possible in its conception.

Numerous public interest groups and researchers have emphasized the need to apply the precautionary principle toward SB, especially in light of the discipline's likely, yet unpredictable and unquantifiable risks (43,48,67,153,161,201,233,254-256). Most SB enthusiasts, however, argue that the precautionary principle is an unacceptable approach to managing the field's emergence in society. Indeed, despite the principle's good intentions, some claim it could, paradoxically, cause harm to the environment and public health by preventing or removing a potentially beneficial product from society (251). Still, others assert the precautionary principle must not be implemented as a means through which to guide the introduction of emerging technologies in society because of its inherent focuses on risk (248,251,257-259). Instead, proponents of the opposing pro-actionary principle assert the discipline's activities should be considered inherently positive and, perhaps not surprisingly, support a minimal form of governance, normally in the form of 'self-regulation' (108,139,233).

As indicated at this study's outset (see sub-section 3.4.1), this study was interested in identifying both the risks *and* benefits a SB product could have on the social well-being of Albertans. As such, while this researcher assumed that the product chosen for assessment would carry at least a slight potential to cause Albertans' harm, it was also just as likely to cause them benefit. In the end, while this author approached the research under the position that precaution should be taken when developing and marketing SB products, the precautionary principle was not necessarily followed.

4.4 CHAPTER SUMMARY AND MOVING FORWARD

This scoping exercise was carried out to help identify key sources of information published in three, targeted, topic areas of relevance to this study:

1) 'Scoping' or surveying SB *product visions*,
2) Identifying SB *products* of relevance to Alberta, and
3) Assessing the potential impacts the discipline's *envisioned products* might have on a population using proactive technology assessment.

In the end, this author identified **two** main knowledge gaps within the first and third topic areas listed above. **First**, no previously published studies have attempted to transparently, and systemically, identify what SB products have been envisioned over time. **Second**, while one study (198) was found to have performed an predictive assessment whose broad-reaching aims were similar to that of this study, its lack of methodological detail about how to achieve results created a knowledge gap that required further exploration on the part of this researcher. In addition to having identified these two gaps in knowledge, this scoping review identified key information that could be used to pinpoint an envisioned SB product of relevance to Alberta.

The knowledge gained from this exercise led to a deeper understanding of the key issues related to this research. As such, it helped refine the central research question to focus on two 'subsidiary' research questions, listed as follows:

1) What SB products have been envisioned since the year 2000?

1a) What is the nature of that discourse?

2) Of SB's envisioned products, which might be of particular relevance to the Province of Alberta?

2a) How might an 'exemplar' product of relevance to Alberta impact the social well-being of its citizens?

In the chapter that follows, the methods used to address these questions are described.

CHAPTER 5: STUDY METHODOLOGY

The previous chapter presented the findings of a broad-reaching scoping review. The present chapter describes the methods used to address the two subsidiary research questions that emerged from the previous chapter.

5.1 INTRODUCTION

This chapter is organized into four subsequent sections. Section 5.2 describes the methods used to address research questions **research question 1 and 1a**. Next, section 5.3 addresses the methods used to identify an envisioned SB product of relevance to Alberta (**research question 2**). In the following section (5.4), the methods used to develop (sub-section 5.4.1) and undertake (sub-section 5.4.2) the study's upstream product assessment are discussed (**research question 2a**). The final section (5.5) presents a chapter summary.

5.2 IDENTIFYING AND CHARACTERIZING ENVISIONED SB PRODUCTS AND RELATED DISCOURSE

In chapter four, a scoping exercise was undertaken to help guide, focus, and inform the undertaking of this research. In this chapter, the same methodology was used to identify the range of envisioned SB products discussed in literature, and to conceptualize the nature of discussion around the products and application areas that were identified. In the paragraphs that follow, the methodology used to achieve these goals is described.

5.2.1 SCOPING REVIEW STAGES

This scoping exercise was carried out using the methodological framework previously outlined by Arksey & O'Malley (133). Briefly, this review was carried out in four main stages: **1)** relevant literature was identified and **2)** selected by applying a series of inclusion criteria, **3)** relevant data was then charted (documented) and finally, **4)** the results were collected, summarized, and reported. Sub-sections 5.2.2 to 5.2.4 describe the methods used to address the scoping review's first, second, and third stage, respectively. Stage four will be addressed in chapter six.

5.2.2 IDENTIFICATION AND RETRIEVAL OF LITERATURE

Protocol-based searches were used to identify four main types of documents for review, including: peer-reviewed journal articles, magazine and newspaper articles, as well as governance reports published by non-governmental (NG) and governmental (GOV) organizations. Searches took place over a period of three weeks beginning mid January, 2011. Literature retrieval procedures for each type of document are highlighted in the sub-sections that follow.

Peer-reviewed Literature

Protocol-based searches were used to retrieve English-language journal articles published on SB between the years 2000 and 2010, inclusive. Twelve databases (Annual Reviews, ABI Inform Trade & Industry, BIOSIS Previews, Agricola, Communication Abstracts, Compendex, EMBASE: Excerpta Medica, Environment Complete, Global Health, ISI Web of Science, Ovid Medline, Petroleum Abstracts, and Sociological Abstracts) were searched using the terms "synthetic biology" and "synthetic genomics".

The types of databases selected for searching were informed by the results of the scoping review completed in chapter four, which provided insight into domains wherein envisioned SB products might someday impact (*e.g.* industry, medicine, and the environment). Ultimately, the selection of databases was completed with the help of a research librarian competent in scoping review methodology. Personal knowledge of three journals (IET Synthetic Biology, IET Systems Biology, and Systems and Synthetic Biology) that publish exclusively or extensively on SB resulted in hand searches of each for relevant articles.

Magazine and Newspaper Articles

Initially, four databases (Academic Search Complete, Newspaper Source, Canadian Newsstand, and ABI Inform) were searched for English-language articles published between the years 2000 and 2010, inclusive, containing either the term “synthetic biology” or “synthetic genomics”. Again, a research librarian informed the selection of the databases searched. After an initial scan of the documents retrieved, the Dow Jones Factiva database was searched for additional articles published in a major United Kingdom-based newspaper, The Guardian, using the same search protocol previously described. This was done to supplement the small proportion (10/152, 7%) of United Kingdom-based newspaper articles retrieved during initial searches.

Governance Reports

An inventory of governance documents, previously assembled by the Woodrow Wilson International Center for Scholars (260), was drawn upon to compile an initial list of governmental and non-governmental organizations known to publish on SB. To ensure this list was up to date, three additional searchers were performed in Google using the constructs:

- “synthetic biology” **OR** “synthetic genomics” **AND** policy
- “synthetic biology” **OR** “synthetic genomics” **AND** governance, and
- “synthetic biology” **OR** “synthetic genomics” **AND** report

Searches continued until no new organizations were identified on two consecutive results pages (10 results per page). Following these procedures, a final list of organizations was compiled (Table A.1) and each of their Websites located. Next the terms “synthetic biology” and “synthetic genomics” were entered into each website’s search bar and search results were scanned for published governance documents (.pdf format). Two additional websites

(Canadian Public Policy Collection and PolicyDocs.com) were also searched for governance documents following the same procedure.

5.2.3 DATA MANAGEMENT AND INCLUSION CRITERIA

Documents were included for review if they: **a)** were available electronically in full-text and readable in ATLAS.ti qualitative content analysis software, **b)** were published in the English language between the years 2000 and 2010, inclusive, **c)** contained either the term "synthetic biology" or "synthetic genomics" in the article's main text, and **d)** explicitly and unambiguously mentioned at least one envisioned SB product (*e.g.* re-engineered microbes that produce hydrocarbons) or potential application area (*e.g.* energy or agriculture). Note that only documents available in full-text at the time of this review were considered. Ultimately, this process entailed screening documents at three levels, described in further detail as follows.

Levels of Screening

RefWorks (261) web-based bibliographic software was used to manage the **first** level of screening for inclusion, which involved the identification and removal of duplicate articles as well as articles that were published in a foreign language, those published outside the desired date range (2000-2010, inclusive), and article **type**. Briefly, news summaries, book reviews, newsletters, conference/meeting papers, journal previews and editorials were excluded from review. Further, reports that did not devote a substantial proportion (at least one paragraph) of their content to policy or governance matters related to SB were also excluded[18]. All articles

[18] For example, two reports conducted by Peter D. Hart Research Associates (on behalf of the Woodrow Wilson International Center for Scholars) (46,528) and one by the Royal Academy of Engineering (47), discussed public dialogue surrounding SB in the United States and the United Kingdom. While each of these reports mention or discuss at least one envisioned SB product, the amount of content devoted to SB policy or governance matters was negligible. As such, they were excluded from review.

were screened for inclusion twice by this author and no discrepancies in inclusion were noted at this level.

All documents that remained after the first level of screening were provided a unique identification number and were subsequently screened for inclusion at a **second** level. This process involved the following procedure: all articles were scanned for the presence of the term “synthetic biology” **or** “synthetic genomics” in their **main text** using the using the control + F or ‘find’ function available in Microsoft Office. Of note: if the term “synthetic biology” or “synthetic genomics” was located in an article’s title, reference list, keywords, or abstract, but **not** its main text, it was excluded from further review. Again, all articles were screened for inclusion twice at this level and no discrepancies were noted.

Documents that remained after the second level of screening were then scanned for inclusion at a **third** and final level. This involved locating articles that mentioned or discussed at least one envisioned SB product **or** application area wherein an envisioned SB product(s) could someday be used. To facilitate this process, each document was searched for the terms ‘product’, ‘future’, and ‘application’ using the ‘find’ function described previously. If articles were found to be includable based on those searches, their identification numbers were recorded in a Microsoft Excel spreadsheet for future reference. Articles that were not deemed includable based on those searches were scanned individually by full text for the presence of an envisioned SB product or application area. If they were deemed includable based on that process, their identification numbers were also recorded in the Microsoft Excel spreadsheet referred to previously.

All articles whose identification number was recorded in the Microsoft Excel spreadsheet (hereafter referred to as the ‘article logbook’) were screened for inclusion twice by this author using the same processes described previously. Once a second screening was completed, discrepancies in article inclusion were found in 3% (n=21) of articles. Those discrepancies were resolved with the help of a disinterested observer who independently reviewed the articles in question using the criteria described previously. Once that process was complete, the second reviewer's conclusions about each article's inclusion were compared to this author's conclusions and the results were discussed until a consensus was reached. In the end, a total of n=697 articles were deemed initially eligible for review. Table A.2 shows a numerical breakdown of articles excluded by type. It also highlights the number of articles initially deemed eligible for review as well as the *actual* number of articles reviewed, discussed in further detail as follows.

Final Selection of Articles

All of the reports (n=26) considered eligible for review were included for analysis in the scoping study. Due to the large volume of magazine and journal articles deemed initially eligible for review, only a portion was selected for actual review. To narrow the number of documents analyzed without sacrificing the results, a random, stratified, sample of magazine and journal articles was selected using a random number generator (Microsoft Excel) created by this author. This process was carried out for magazine and journal articles as follows.

Magazine Articles: Each of the magazine articles initially considered eligible for review (n=240) were first grouped by: **a)** magazine type (trade magazine, news magazine, *etc*...), then by **b)** content type (chemical engineering, pharmaceutical science, business, *etc*...). Next, one article was randomly selected from each 'content type' group using the random number generator described previously. Once one article was selected from each group, their content was analyzed and a decision was made as to whether data saturation had been reached[19]. In this study, multiple rounds of article selection were undertaken before this author was satisfied that data saturation had been reached. In the end, this process resulted in n=90 magazine articles having been included in the review.

Journal Articles: Each of the journal articles initially considered eligible for review (n=275) were grouped by the type of content published by the journal (physics, plant biology, chemical engineering, *etc*...). Next, one article was randomly selected from each group of articles using the random number generator described previously. Once articles were selected, their content was analyzed and a decision was made as to whether data saturation had been reached. In this study, multiple rounds of article selection were undertaken before this author was satisfied that data saturation had been reached. In the end, this process resulted in n=96 journal articles having been included in for review.

Of the newspapers originally considered eligible for review (n=221), 17 sets (a total of n=66 articles) contained virtually identical content, but were published as separate articles across a variety of Canadian newspapers. To avoid analyzing identical content, one article was randomly selected from each of the 17 sets of articles using the random number generator described previously. In the end, a total of n=155 newspaper articles were included for review.

5.2.4 CHARTING RELEVANT DATA: EXTRACTION, COMPILATION, & SYNTHESIS

Three types of information were extracted from the articles included in this study: **1)** simple publication details, **2)** envisioned SB products and/or application areas, in addition to **3)** the nature of discourse surrounding them. Two 'codebooks' containing a list of all variables of interest to this study were prepared prior to commencing the analysis (262,263). These

[19] In this study, data saturation referrers to the point at which this researcher no longer saw new information emerge from the data

standalone documents explained how and where the variables or 'codes' of interest were to be measured and recorded. In this study, two codebooks were created. The first codebook (Table A.3) pertained to the identification of simple publication details, which were to be recorded in the study's logbook. The second codebook (Table A.4) pertained to the identification of envisioned SB products and application areas, as well as the nature of discourse surrounding them. This information was collected by employing qualitative content analysis methodology and was facilitated by the use of ATLAS.ti (264) qualitative content analysis software.

Given the integral role that qualitative content analysis research methodology played in this study's data collection process, it is discussed in further detail in the section that follows.

Qualitative Content Analysis

Content analysis (CA), a research technique used to systematically examine the content of virtually all types of communication (*e.g.* auditory and written (265)), was used to synthesize the content of material included in this review. Often dichotomized into two main types, 'quantitative' and 'qualitative' (266) content analyses differ in the fundamental approaches used to analyze communication content: primarily numerical and objective (quantitative), and primarily non-numerical, subjective, and descriptive (qualitative) (265,267). In this study, a *qualitative* approach to data analysis was employed.

Hsieh & Shannon (266) have described three distinct approaches to qualitative content analysis, namely: conventional, directed, and summative. In conventional content analysis, coding categories are not pre-conceived, but are derived from the data, much like the approach used in grounded theory[20] (266). Under a directed content analysis approach, the initial

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[20] As described in section 3.6, unlike content analysis studies, Grounded Theory (GT) research is generally 'theoretically founded'; *i.e.*, researchers generally choose a specific conceptual, philosophical, or highly abstract framework or system through which to describe events (171). Further, the general goal of GT studies is the development of a theory (or theories) that is 'grounded in' or heavily connected to the data collection and analysis

selection of codes is based on previous research and/or theory (266). Following the 'summative' approach to content analysis, the frequency with which key terms or topics of interest are mentioned is determined (manifest coding) in addition to the nature of discussion surrounding that discourse, such as emerging themes (latent coding) (266). In this study, the *summative* approach to content analysis was implemented, and thus, both manifest and latent coding procedures were employed during the data collection process. These procedures are described in further detail in the section that follows.

The manifest and latent coding process

Coding is a process whereby one or more researchers systematically examines identical pieces of raw communication data, normally by following the protocol set in a codebook, and (ideally) assign the same meaning to it (268). It is a process that ultimately allows larger units of data to be aggregated into meaningful units of data that allows a more precise description of relevant characteristics (269). With the assistance of ATLAS.ti (264), manifest coding allowed each unit of analysis (an envisioned SB product(s) and/or potential application area) to be recorded, and thus, to become quantified. Using the same software, latent coding was employed to facilitate the recognition of patterns and themes that emerged around those units of analysis (270).

As an iterative process, this study's latent coding process involved the constantly comparing new codes to those that had already been found (271,272). As such, emerging themes and patterns were constantly compared and refined as necessary. Memoing was also undertaken, *i.e.,* this researcher recorded and elaborated on thoughts and ideas that emerged

process (529). In this qualitative content analysis study, the aim was not to develop a theory to explain a particular phenomenon, but rather, to produce a basic thematic description of the data collected.

throughout the analysis (270). To ensure that the themes and categories that emerged were as transparent as possible, an effort was made to ensure that data was organized in a manner that allowed it to be traced back to its original source (265).

In its role as 'research assistant', ATLAS.ti Version 6 (264) proved invaluable throughout this study's manifest and latent coding processes. This software allowed coding to be more consistent, less tedious, and conducted at a faster pace than would have been possible if manual coding was used (269,273). While valuable, however, this researcher did not consider ATLAS.ti as a substitute for human thought and intellectual input (269,273,274). Indeed, although the program was useful in helping locate and quantify the occurrence of coding units and grouping content into specific categories of interest, only human insight on the part of this researcher was able to evaluate the context of content being examined (265,274,275).

Data compilation and synthesis

The manifest and latent content extracted and analyzed in this study was compiled and synthesized as follows. The results of the manifest coding process (identified using ATLAS.ti) were printed and each coding unit (envisioned SB products and potential application areas identified) was manually entered into the study's logbook by this researcher. During this process, each coding unit was differentiated and grouped by *type*. Once this process was completed, all of the products listed in each group were counted twice by this author. No numerical discrepancies were identified.

To ensure that envisioned products had not been overlooked during the first round of coding, this author coded each article a second time. The results of the second round of coding were printed and compared with the results of the first round of coding. Any product that had been overlooked during the first round of coding was added to the study's logbook and this author completed two *final* counts. Again, this researcher did not identify any discrepancies in product count during this process.

The latent content coded in ATLAS.ti was printed and emerging themes and patterns were constantly compared and categories were refined as necessary. In the end, this process allowed for the identification of several emergent themes[21] pertaining to envisioned SB product discourse. To ensure that the themes identified by this author were based on sound reasoning, this author provided a second reviewer (the supervisor) with the themes that emerged from the process, and justification as to how those themes were chosen. The supervisor reviewed the themes and did not identify any issues.

5.2.5 STUDY QUALITY

In qualitative research, a trustworthy (high quality) study is determined by the persuasiveness of the work presented, *i.e.,* whether the raw data supports the study's conclusions (270). Lincoln & Guba (276) describe a trustworthy study as one that has established credibility, dependability, confirmability, and transferability (270,276,277), each of which is examined in further detail in the discussion that follows.

If a qualitative study has credibility, a researcher is able to demonstrate that the findings they report are a true representation of the data that was scrutinized. Indeed, the research focus and approaches should be made explicit from the onset and the data analysis process should be undertaken in a systematic, transparent, and rigorous fashion and in clear relation to the study design (4,277-279). In this study, two main steps were undertaken to increase credibility. First, in order to make judgements about the similarities and differences within and among coding categories, during the identification of emerging themes, 'exemplar'

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[21] Frequently recurring categories of data representing similar subject matter (266)

statements (specific quotations that illustrated representativeness within themes were established. Second, the supervisor reviewed the study's findings in an attempt provide a 'check' for items that might have been either selectively perceived or missed by this researcher. This approach, used to verify that an account being reported is robust, comprehensive, and well-developed, is referred to as analyst triangulation (279,280).

Following qualitative research tradition, the findings of a study are considered dependable if they are consistent with the data from which they were gathered and can be repeated (277). To increase the dependability of this study, an 'external audit' was undertaken by the supervisor (281). In the role as external auditor, the supervisor examined the processes undertaken to analyze the data as well as the study's findings and evaluated whether the interpretations and conclusions were indeed supported by the data (282,283).

A study's confirmability relates to the objectivity or neutrality with which a study has been undertaken (270). If a study has confirmability, there is consistency between the researcher's conclusions and the observations from which they were drawn (270). Indeed, the study's findings should not be shaped by researcher bias or self-interest, but rather, the data itself. Two main approaches were taken to increase the confirmability of this study. First, a clear and transparent description of the study's research path 'audit trail' was maintained from the onset (281). Second, knowing that a variety of factors, such as personal values, experiences, beliefs, and research perspectives might have played a role in how the data was approached and interpreted, reflexivity (explicit declaration of these factors) was employed throughout the research process (281).

In qualitative research tradition, a study's transferability refers to the extent within which its findings can be applied to other contexts (time, setting, and situation) or groups of data (270,281). Ultimately, the level of a study's transferability is judged by the reader, but the researcher normally employs specific strategies to help achieve it. In this study, a robust or 'thick' description of data collection methods, analysis procedures, and study findings was presented in hopes that the reader would have an adequate amount of information upon which to judge this study's transferability (277,281).

This section outlined the methodology undertaken to address research question 1. In the following section, the methods used to address research question 1a are described, specifically, *which of the envisioned products identified during the scoping process might be of particular relevance to the Province of Alberta?*

5.3 IDENTIFYING AN ALBERTA-RELEVANT 'EXEMPLAR' PRODUCT

Information from the conceptual framework (particularly, Table 3.1) and the scoping exercise performed in chapter four (in particular, section 4.3.2) was used to help identify an envisioned SB product of relevance to Alberta. Briefly, products identified during the scoping review were scrutinized against four elements: **1)** Alberta's current and historic SB research activities, **2)** the province's political and economic landscape, **3)** public support for specific SB products, **4)** and Alberta's research investment and innovation priorities. Ultimately, the product that aligned best with those elements was subjected to the study's upstream product assessment.

Now that the methods used to identify the Alberta-relevant product have been established, the process undertaken to address the study's central research question: *how might synthetic biology's envisioned products impact the lives of Albertans?* will now be addressed (section 5.4)

5.4 UPSTREAM PRODUCT ASSESSMENT

To help understand how an Alberta-relevant envisioned SB product might someday impact the social well-being of Albertans, an upstream product assessment (UProd) framework needed to be developed and then applied. In sub-section 5.4.1, the methods used to develop the UProd are discussed. Following this, sub-section 5.4.2 discusses the methods used to apply the framework.

5.4.1 DEVELOPMENT OF THE UPROD

The main source of information used to develop the UProd framework was the scoping exercise described in chapter four; in particular, the six elements contained in Table 4.4. Briefly, each of those elements' relevance to the study was considered; a process that was guided by drawing upon the ideas and assumptions described in the study's conceptual framework. Ultimately this process made possible the selection of a focused number of elements that aligned best with the study's research goals:

- Implications of replacing a conventionally used counterpart,
- Historical experiences of similar technologies,
- Selection of stakeholders, and
- Ethical, environmental, and economic implications

Once relevant elements were selected to form part of the assessment framework, broader considerations were made about *how* and *when* each of those elements should be considered during the assessment process. In the end, this researcher decided that the UProd would be comprised of two main components. The **first component** would act as an 'assessment orientation' process, and involves two components, which include:

1) identifying a conventionally used counterpart to the SB product being assessed, then considering the implications (pros and cons) of replacing that conventionally used counterpart with the envisioned SB product in question, and
2) identifying an existing technology similar to the SB product being assessed, then considering what oversight and regulatory issues experienced by that technology might be useful in helping guide the execution of the UProd assessment within the context of the SB product in question.

The **second component** of the framework would first involve the identification of relevant stakeholders that could be impacted by the envisioned SB product. Once relevant stakeholders were identified, this researcher felt it pertinent to address economic and environmental implications separately from ethical implications. As such, the second component of the UProd assessment framework consisted of two 'assessment matrices': one matrix that addressed **social** implications (economic and environmental) on the stakeholders chosen, and the other addressed the **ethical** implications on stakeholders. When attempting to identify ethical implications within this context, this author used Mepham's approach to ethical analysis (246).

Together, the two components described in the present section formed this study's UProd framework. In the sub-section that follows (5.4.2), the methods used to implement the framework are discussed.

5.4.2 Implementing the UProd

A variety of information sources were drawn upon during the implementation of this study's upstream SB product assessment framework, including: peer reviewed literature, governance reports, government websites, as well as information obtained from this study's two literature scoping exercises. The type of literature sought, and the manner in which it was sought, depended upon the element being considered. In this study, the exemplar product chosen to undergo assessment was re-engineered microbes designed to produce bio-butanol transportation fuel. As such, the sources of information for each element of the frameworks' dimensions, the rationale for using those sources, and the corresponding search methods to identify information from within those information sources, are described in further detail in Table 5.1 as follows.

TABLE 5.1 SOURCES OF INFORMATION, RATIONALE, AND METHODS SOUGHT

Information Source & Rationale	Information Search Methods
Identifying a conventionally used counterpart	
• Scoping review results indicated that fossil fuel derived gasoline fuel would serve as an adequate conventionally used counterpart with which to compare bio-butanol transportation fuel derived from re-engineered microbes	• Used information mainly obtained from documents analyzed during the literature scoping process
Historical experiences of similar technologies	
• This author's personal knowledge directed searches toward industrial biotechnology as a relevant historical technology for reference • The Industry Canada website was scanned for relevant information pertaining to regulation and oversight within the industry • During the scoping review, this author noted discussion surrounding the 'familiarity principle', which was also considered relevant	• Industry Canada website was located and scanned for relevant information. If relevant links were provided to other websites of interest, they were followed. Searches continued until this researcher was satisfied that no new information was relevant • SB governance and policy reports identified for review during the scoping review (chapter four) were searched for the term 'familiarity principle'. Relevant results were collected.
Selection of stakeholders	
• Several stakeholders were based on personal conjecture and choice of feedstock used to 'fuel' the bio-butanol producing microbes	• Personal conjecture and information retrieved from chapter four re: Bio-conversions network work on creating re-engineered microbes capable of living off Alberta- grown crops
Social (environmental and economic) implications	
• Scoping reviews (chapter four and five) provided initial information on this matter • Supplemental information was sought by searching Google, Google Scholar, and Web of Science	• Search terms used to collect information from electronic databases included: • Biofuel AND environment; biofuel AND economy; biofuel AND environment OR economy AND implication OR impact • Searches continued until this researcher was satisfied that no new information was relevant
Ethical implications	
• Scoping reviews (chapter four and five) provided initial information on this matter • Supplemental information was sought by searching Google, Google Scholar, and Web of Science	• Search terms used to collect information from electronic databases included: ○ Ethic AND biofuel; ethic AND biofuel AND implication OR impact • Searches continued until this researcher was satisfied that no new information was relevant

Once the information gathering process was complete, the social and ethical implications that bio-butanol produced by re-engineered microbes could have on the social well-being of Albertans were revealed.

5.5 Chapter summary

This chapter described the methods used to address each of the study's three research questions. First, it described the methods used to scope SB discourse for envisioned SB products (section 5.2). Second, in section 5.3, it described the methods used to determine what envisioned product might be of particular relevance to Alberta. Next, this chapter discussed the methods used to address the study's central research question (section 5.4). In the chapter that follows (six), the findings that emerged from the application of these methods to the study data are described.

CHAPTER 6: FINDINGS

The previous chapter outlined the methodology used to address the study's research questions. This chapter presents the findings that emerged from the data as the methods were carried out.

The present chapter is divided into five main sections. The first section (6.1) describes the findings of the scoping review, while section 6.2 discusses the Alberta-relevant 'exemplar' product chosen for upstream assessment. The third section (6.3) presents the study's completed UProd, and in section 6.4, the findings that emerged from the implementation of that framework are provided. The chapter is then concluded with a brief chapter summary (section 6.5).

6.1 SCOPING REVIEW FINDINGS

This section presents the findings of the scoping review and is divided into three main sub-sections. The first sub-section (6.1.1) provides the descriptive characteristics of the articles included for analysis. In sub-section 6.1.2, the findings that emerged on each type of envisioned product are presented. The final sub-section (6.1.3) presents the major themes that emerged during an analysis of the product vision discourse.

6.1.1 DESCRIPTIVE CHARACTERISTICS

A total of N=2847 magazine and newspaper articles, peer-reviewed journal articles and reports were initially identified from systematic searches of electronic databases, SB journals, and governmental and non-governmental organization web pages. After scanning for inclusion, n=2150 articles were excluded from full review, including n=480 (17%) articles because they did not discuss an envisioned SB product or application area. This left a total of n=696 (24%) articles eligible for analysis. With all eligible reports, newspaper articles, and a random selection of magazine and peer reviewed journal articles chosen for review, a total of N=367 documents were analyzed at the full text level (Figure 6.1). A more detailed numerical breakdown of articles *excluded* from review is provided in Table A.2.

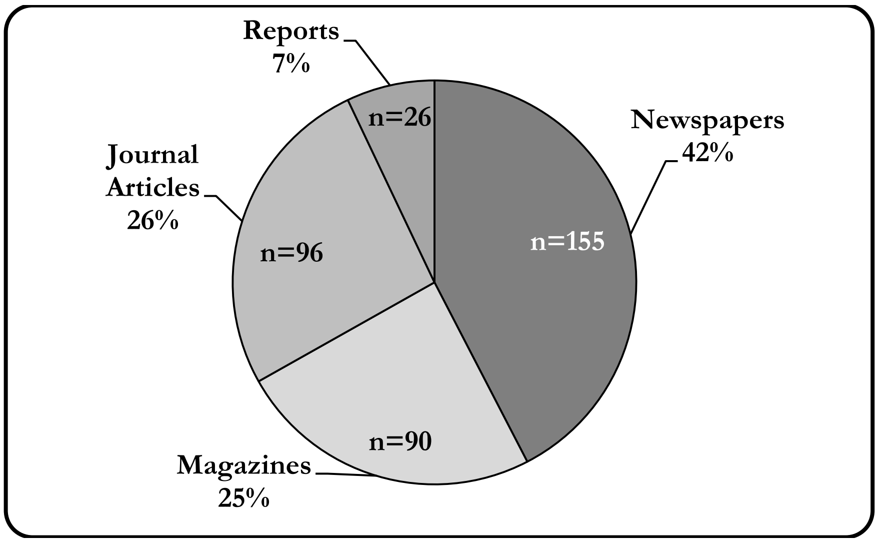

FIGURE 6. 1 NUMBER OF DOCUMENTS INCLUDED FOR REVIEW, BY TYPE

As mentioned previously, of the articles initially identified, a total of n=696 (24%) were considered 'includable' because they mentioned at least one envisioned SB product or application. By contrast, n=480 (17%) of articles were deemed ineligible for review because they did not. Figure 6.2 compares these two groups by illustrating the percentage of articles that were included across all article types, by publication year.

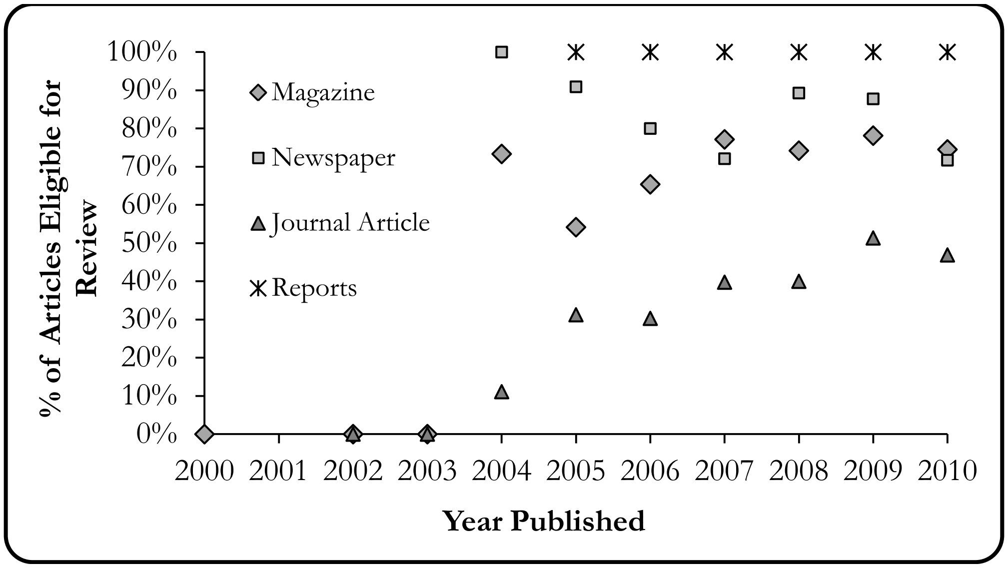

Figure 6. 2 Percentage of articles that mention envisioned SB products, by publication year

The percentage of journal articles that mentioned or discussed envisioned SB products showed a tendency to increase over time (Figure 6.2). By contrast, the percentage of popular media (magazine and newspaper) articles did not show a clear tendency to mention or discuss envisioned products over time. Overall, those articles tended to mention or discuss envisioned SB products or potential application areas more than 50% of the time. All reports that entered the second phase of inclusion screening mentioned or discussed at least one envisioned SB product.

Countries of Origin

The geographical origin of reports as well as journal, newspaper, and magazine articles analyzed in this study is shown in Figure 6.3. Nearly half (47%) of articles originated in the United States and 18% each originated in the United Kingdom and Canada. The n=39 'other' countries represented by documents analyzed in this study are identified in Table B.1 (Appendices).

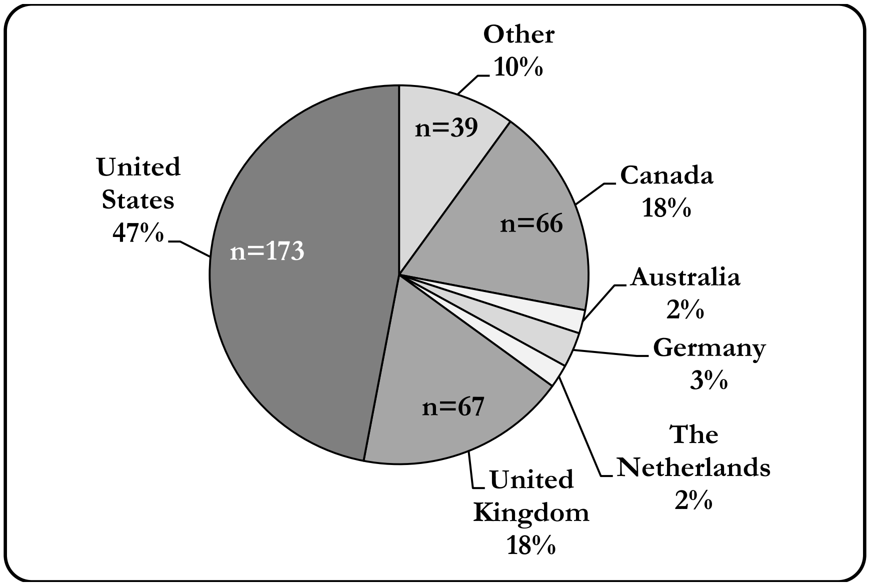

FIGURE 6. 3 INCLUDED ARTICLES' COUNTRIES OF ORIGIN

Publication Dates

As illustrated in Figure 6.4 (follows), the number of articles included in this review generally increased each year from 2004 to 2010, inclusive.

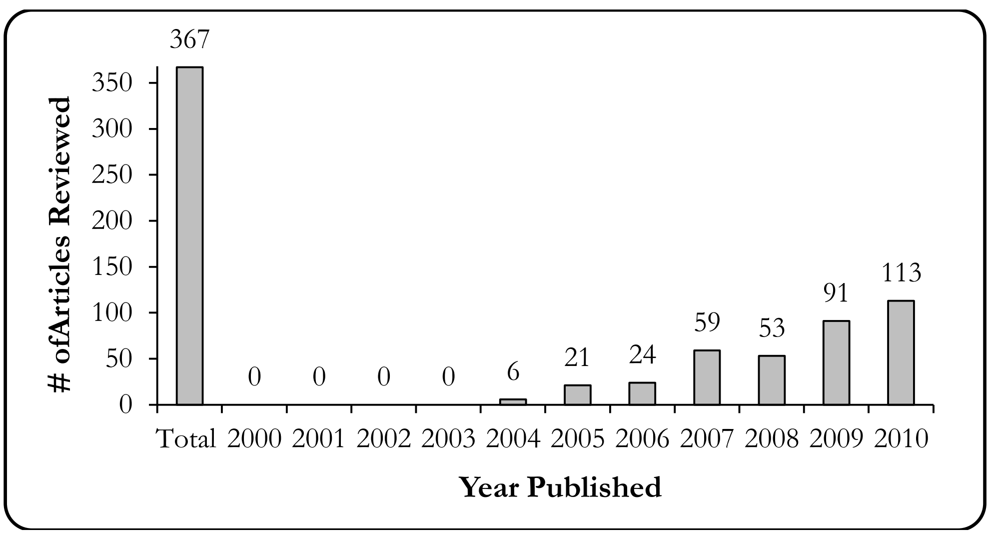

FIGURE 6. 4 NUMBER OF ARTICLES REVIEWED, BY PUBLICATION YEAR

Now that the articles' descriptive characteristics have been presented, this chapter moves forward to present the types of envisioned SB products that emerged during the scoping process (sub-section 6.1.2). Several 'timeline' predictions pertaining to *when* those product visions might become realized were also identified. This information will be presented at the end of section 6.1.2.

6.1.2 Envisioned Synthetic Biology Products: Application Areas Differentiated

A total of N=117 distinct envisioned SB products were discussed across the documents analyzed, all of which have been differentiated into eight main 'application areas' (Table 6.1).

Table 6. 1 The eight application areas of envisioned SB products identified in the literature

Envisioned Application Area	# Articles & Reports (%)
Renewable Energy	288 (78%)
Alternative Bio-fuels	*277 (75%)*
Bio-electricity	*11 (3%)*
Physical[A] Health	257 (70%)
Human	*252 (67%)*
Veterinary	*5 (1%)*
Industry	154 (42%)
Environment	111 (30%)
Food	39 (11%)
Agriculture	35 (10%)
Defence	25 (7%)
Science Fiction/Fantasy	15 (4%)
Total # Articles Reviewed	**367 (100%)**

[A] In this section, the term 'physical' has been omitted from the term 'health' for the sake of brevity

Energy and health related products were the most widely mentioned or discussed types of envisioned SB products across the literature reviewed. By contrast, envisioned defence and science fiction/fantasy products were mentioned or discussed in the least number of articles (seven and four percent, respectively) (Table 6.1). In the sections that follow, the types of products identified within each of the application areas will be discussed in further detail.

Envisioned Renewable Energy Applications

As shown on Table 6.1, two types of renewable energy applications were identified during the scoping process: the production of alternative bio-fuels (mentioned or discussed in n=277 articles) as well as the production of bio-electricity (n=11 articles). In the two sub-sections that follow, the findings relating to these two types of applications will be explored in further detail.

Alternative Bio-fuels

"Genetically engineered microbes will eat sugar and crap oil" - David Roberts, Grist Magazine

Described as the "killer app" and "holy grail" of SB (203), the production of <u>renewable energy</u> was the most frequently discussed envisioned SB application area across the documents reviewed. Indeed, three quarters of the articles included for review (n=277 or 75%) either mentioned, or discussed, the possibility for SB to be used for this purpose. Across all document types, more than half either mentioned or discussed SB's future role in energy production (Figure 6.5).

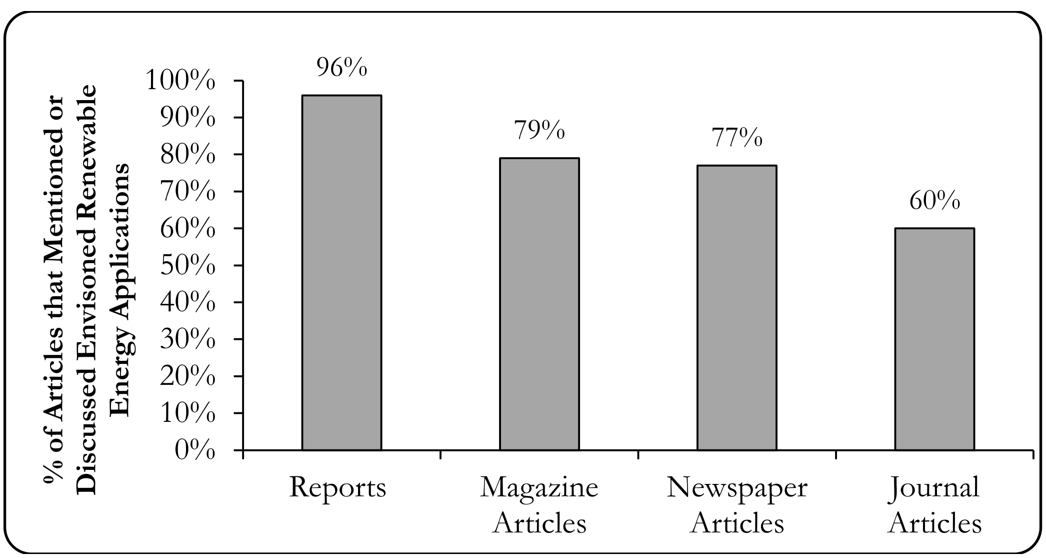

FIGURE 6. 5 PERCENTAGE OF ARTICLES THAT MENTIONED OR DISCUSSED SB'S FUTURE ROLE IN RENEWABLE ENERGY PRODUCTION

In documents that mentioned or discussed SB's possible role in the energy industry, 78% discussed the possibility of re-designing microbes to produce a specific type of liquid energy product (Table 6.2). All but one (bio-methane) were transportation fuels.

TABLE 6. 2 ENVISIONED SB ENERGY APPLICATIONS

Type of Energy Product	**# (%) Articles within which Product was Mentioned or Discussed***
Bio-Butanol	n=25 (9%)
Bio-Diesel	n=44 (16%)
Bio-Ethanol	n=67 (24%)
Bio-Hydrogen	n=53 (19%)
Bio-Jet Fuel	n=27 (10%)
Bio-Methane	n=2 (0.7%)
Fuels in General	n=61 (22%)
SB's Potential Role in Energy Domain	**N=277 (100%)**

* Articles that discussed more than one product were included multiple times

As illustrated in Table 6.2, of the n=277 articles that mentioned or discussed SB's potential role in the domain of alternative bio-fuels, the most widely discussed product was microbes re-designed to produce bio-ethanol (24%). Microbes re-designed to convert underground coal reserves into methane gas were mentioned in the fewest number of articles (n=2) (153,284).

Along with mentioning or discussing potential envisioned products, many articles also provided a variety of rationales relating to the *need* to produce SB energy products. In the section that directly follows, the themes that arose from this discussion are addressed.

Rationalizing 'synthetic' energy products

While forty years ago the need for alternative fuels might not have seemed urgent, today the literature revealed the need is greater than ever. With dwindling fuel supplies, increasing global energy demands and oil prices, and concerns about the environmental impact associated with their retrieval and usage[22], there have been increased calls to find replacements for 'dirty' fossil fuels in lieu of 'cleaner' energy sources that carry a more acceptable environmental impact (178,285,286). Described as the "number one problem facing the planet" (287), SB has been given a great responsibility by many of its proponents: solving the world's energy crisis (254) with applications that could someday "save the planet" (288).

During the course of the analysis, this author noted five frequently discussed motivations behind the use of SB to produce alternative sources of energy. These included: **1)** economic, **2)** geo-political, and **3)** environmental **4)** regulatory motivations as well as **5)** public opinion. Due to the extensive discussion devoted to these issues, each of these motivators has been highlighted in some detail in Table 6.3, as follows.

[22] When combusted for energy use, all fossil fuels produce carbon dioxide, a greenhouse gas believed to contribute to global warming (530)

TABLE 6. 3 FIVE BROAD MOTIVATORS BEHIND THE USE OF SB IN THE PRODUCTION OF ALTERNATIVE ENERGY

Type of Motivation	Details
Economic	
Cost Effectiveness (n=6) (178,187,289-292)	• With rising oil prices, SB-based bio-fuels could become an inexpensive alternative to fossil fuel production. • SB-based production of bio-hydrogen and ethanol could save approximately $20 billion a year in fossil-fuel related costs over the next 50 years
Market Potential (n=6) (139,254,286,288, 293,294)	• Fossil fuels are non-renewable, and thus un-sustainable: their supply will begin to decline at some point • Given the world's current dependence upon fossil fuels, stricter government regulation around greenhouse gas emissions, and that and the energy market is larger than many other biotechnology markets (e.g. bio-pharmaceutical), SB-producing microbes that are set to replace conventional liquid energy products could someday be worth trillions of dollars. • Several 'Big Oil' companies have begun investing in SB's bio-fuel producing future (section B.2), making SB-based bio-fuel production closer to commercialization than some others. • One of SB-based bio-fuel production's selling points is the ability to use non-food based plant matter as a feedstock; some state this could "rejuvenate U.S. agriculture"
Economic Growth (n=1) (153)	• Nations experiencing energy deficits often have low economic growth and development; synthetic bio-fuels might help overcome these issues
Geo-political	
National Security (n=9) (119,198,203,233, 254,286,295-297)	• Especially in the United States, there is a sense of urgency to reduce foreign dependence on imported oil from the Middle East • SB might someday hold the power to wean the western world from this dependence
Environmental	
Environmental Disasters (n=5) (153,233,295,298, 299)	• Unlike fossil fuels, many bio-fuels are bio-degradable; if accidentally released, most would not cause long-term environmental damage. • Lessening the exploration of fossil fuel 'drillables' can prevent oil spill disasters such as the 2010 BP oil spill in the Gulf of Mexico • With SB, only desired chemicals can be created, avoiding unwanted "mixtures of tars and toxins" (299) that have to be dealt with during the oil refining process **(Cont'd)**

TABLE 6. 3 (CONT'D) FIVE BROAD MOTIVATORS BEHIND THE USE OF SB IN THE PRODUCTION OF ALTERNATIVE ENERGY

Type of Motivation	Details
Environmental	
Addressing Global Warming (n=7) (187,233,254,295, 300-302)	• Microbes could be re-engineered to absorb greenhouse gases, such as CO_2, and produce renewable bio-fuels
Regulatory	
Policies, Regulations, & Bills (n=12) (28,187,203,233, 254,295,303-308)	• Several international regulations, policies, and incentives (low carbon policies) aim to cap greenhouse gas emissions and reduce the negative environmental impacts associated with fossil fuels • Examples: o Waxman-Markey Energy Bill: cap greenhouse-gas emissions and allows companies to sell emission savings for credits o The Renewable Fuels Standard mandates the annual growth in gasoline replacement with renewable bio-fuels through 2022
Public Opinion	
(n=6) (48,151,203,295, 298,300)	• Oil spill disasters have renewed public interest in non-renewable fossil fuels, pushing public toward renewable energy

In addition to noting the five interlinked motivations described above, this author also noted frequent discussion surrounding SBs potential *advantages* over conventional bio-fuel production methods. In the section that follows, key findings that emerged from this discussion surrounding are described.

The synthetic biology bio-fuel advantage

Using microbes to produce bio-fuel is not a new concept that emerged with the development of SB. Indeed, conventionally produced bio-fuels (especially bio-ethanol) have been produced and used in the United States and Brazil for several years (309). As noted in the literature, however, one of the major points of contention about 'conventional' bio-fuel production is that food products such as corn (and thus fertile agricultural land) are used to produce it. This diversion of food products into bio-fuel feedstocks has elicited the 'food versus fuel' debate: when food crops are converted into fuel, less food is available for those in need and food staples, such as corn, can become significantly more expensive (198). The literature pointed out that SB could offer solutions to these problems by offering 'advanced bio-fuel' alternatives (104,153,198,203,254,310)[23].

Instead of using food crops to produce bio-fuels, synthetic biologists aim to re-wire (or create entirely new) microbes with the ability to **a)** ferment cellulose from a variety of agricultural waste products (cellulosic fermentation) or **b)** capture energy from the sun (photosynthesis) to produce bio-fuels at a cost that is expected to be lower than, or at least comparable to, current fossil fuels. As shown in Table 6.4, practitioners suggest a variety of host organisms, metabolic methods, feedstocks, and bio-fuels have could be created to produce advanced SB bio-fuels. Discrepancy exists, however, over what options might be the most desirable.

[23] Advantages and disadvantages of conventionally used bio-fuels are described in Table B.4

TABLE 6. 4 ENVISIONED SB BIO-FUELS: HOST ORGANISMS, CORRESPONDING FUEL PRODUCED, AND RELATED CHARACTERISTICS

Microbial Host Details	Characteristics
Bio-butanol (88,153,185,198,311,312)	
Microbial Model: Cyanobacteria (blue-green algae) or anaerobic bacteria **Type of Metabolism**: Photosynthesis or Fermentation **Feedstock**: Sunlight, CO_2 and nutrients *(cyanobacteria)* or cellulose, other sugars present in non-food agricultural items (agricultural waste- straw, corn stalks, wood chips, sawdust, and switchgrass) *(anaerobic organisms)*	• Could use non-food products that grow on non-arable land • Expect cost of production to become comparable to fossil fuels • Photosynthetic production considered "carbon neutral" as CO_2 consumed by organism during metabolism • More compatible with current transportation technologies and infrastructure than ethanol
Bio-diesel (88,108,153,185,198,203,309,312,313)	
Microbial Model: Cyanobacteria or yeast cells (anaerobes) **Type of Metabolism**: Photosynthesis or fermentation **Feedstock**: Sunlight, CO_2 and nutrients *(cyanobacteria)* or sugarcane (*yeast*) Amyris' yeast production method would produce farnesene, which can be converted into combustible fuel similar to diesel	• Produced from a sustainable resource, not plant and animal oils • Expected: less polluting, lower cost (feedstock inexpensive), greater scale of production, more efficient, than conventional bio-fuel production • Photosynthetic production considered "carbon neutral" • Fermentative production (Farnesene): does not contain impurities like plant-derived bio-diesels (engine damage); no sulphur like fossil fuel-based diesel
Bio-hydrogen (48,314,315)	
Microbial Model: Cyanobacteria **Type of Metabolism**: Photosynthesis **Feedstock**: Sunlight and nutrients	• Expected: cheaper production than conventional hydrogen fuel • Bi-product of combustion: water; no fossil fuel produced when burned • Photosynthetic production considered "carbon neutral" as CO_2 consumed by organism during metabolism
Bio-jet fuel (153,316)	
Microbial Model: Cyanobacteria **Type of Metabolism**: Fermentation **Feedstock**: Cellulose Normally, cyanobacteria are photosynthetic. Solazyme has engineered them to grow in the dark and therefore ferment, a reportedly cheaper process than photosynthesis	• Photosynthetic production considered "carbon neutral" • U.S. aviation industry alone uses six billion litres of jet-fuel a month; SB alternative could reduce carbon footprint • More compatible with current transportation technologies and infrastructure than ethanol

Cyanobacteria (blue-green algae) could serve as a microbial model in the production of at least four types of transportation fuels (see Table 6.4). As summarized in Table 6.5, as follows, while their use in energy production carries strengths and weaknesses, their use also presents several threats to the environment.

TABLE 6. 5 STRENGTHS AND WEAKNESSES OF USING CYANOBACTERIA AS A MICROBIAL HOST FOR SB BIO-FUEL PRODUCTION

Strengths (153,182,254,306,316-319)	**Weaknesses** (254,314)
• Create bio-fuels while consuming a greenhouse gas (CO_2) • Versatile organism, well-suited to genetic manipulation, tolerant of adverse weather conditions • Requires only: sunlight, non-potable water, carbon dioxide, and non-agricultural land (ponds or tanks) to grow • Photosynthetic organisms use less resources than land-based plants • Algae is biodegradable: low environmental impact if spilled • Growth: doubles mass daily (corn, by comparison, is a yearly crop)	• Industrial scale-up would require vast amounts of nutrients, fertilizer; not just CO_2 • Algae reportedly consume more water and energy than bio-fuels produced using fermentation of agricultural products (corn, canola, switchgrass) • Algae reportedly produce higher amounts of greenhouse gases than fermentation-based bio-fuel • Given natural strains' role in ecological devastation (algal blooms), genetic alteration could bring unanticipated negative side effects if grown outside in open ponds

Bio-electricity

A total of n=11 (3%) of articles included in this scoping review mentioned the potential application of SB for the production of bio-electricity. Of these, the majority (n=4 or 36%) were journal articles (187,320-322). Three articles each were reports (48,153,254) and magazine (323-325) articles, and only one (326) newspaper article mentioned SB's potential role in this application area. Table 6.6 provides a breakdown of the nature of SB bio-electricity products identified during the scoping process.

TABLE 6. 6 ENVISIONED SB BIO-ELECTRICITY APPLICATIONS

Application Category	Details
Production of Bio-electricity and 'Electro-Biological' Devices	
General Discussion (n=1) (322)	• Using SB, components of cells capable of transferring electrical charges could lead to several types of 'electro-biological' devices capable of producing electricity
Bacterial Batteries (n=3) (48,325,326)	• SB could be used to design and engineer bacterial batteries from re-engineered eel cells or multiple virus genes • Key example: 2009 City College of San Francisco iGEM team's "bacterial powered battery" (327)
Metabolic Elements Required in SB-based Electricity Production	
Various Sources of Energy (n=7) (153,187,254,320, 323-325)	• SB re-engineered cells could be designed to convert solar energy into bio-electricity or oxidize a variety of other substances, such as: o Human and other liquid waste o Biomass (*e.g.* cellulose) o Various types of chemicals, such as acetate
Functional Mechanisms	
Magnetic Fields (n=1) (321)	• Duke University's 2006 iGEM team created 'Bacterial Dynamo': re-engineered magnetotactic bacteria capable of generating electricity by converting bio-mechanical energy into electricity

Envisioned Health Applications

Health applications were the second most frequently discussed type of envisioned SB products identified during the scoping process. A total of n=257 documents (70% of those reviewed) mentioned or discussed at least one SB health application, all of which can be sub-categorized into two main types: a) human health applications (identified in n=252 documents) and b) veterinary health applications, which were identified in n=5 documents. In the two sub-sections that follow, the findings pertaining to these two health product categories are explored.

Envisioned Human Health Applications

"You can fight almost any disease, if you think about it" - 17 year old Sagar Indurkhya, about SB (328)

Across all types of envisioned SB products, those related to human health were the second most popular with 67% of articles (n=252) having either mentioned, or discussed, the possibility for SB to be applied within this sector. Across all document types, more than half of those examined discussed envisioned human health applications (Figure 6.6).

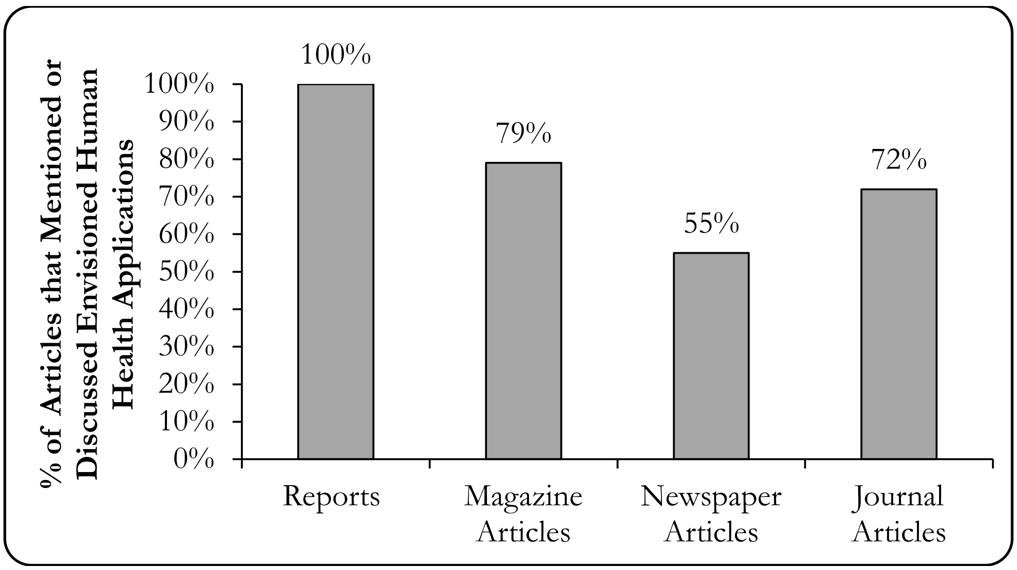

FIGURE 6. 6 PERCENTAGE OF ARTICLES THAT MENTIONED OR DISCUSSED SB'S FUTURE ROLE IN HUMAN HEALTH

In documents that mentioned or discussed one or more human health applications, most discussed the discipline's future role in drug production (Figure 6.7). Of these, 38% discussed the production of the anti-malarial drug Artemisinin (see chapter two for background). Figure 6.7 provides a breakdown of the five types of envisioned human health application areas for SB identified during the scoping process.

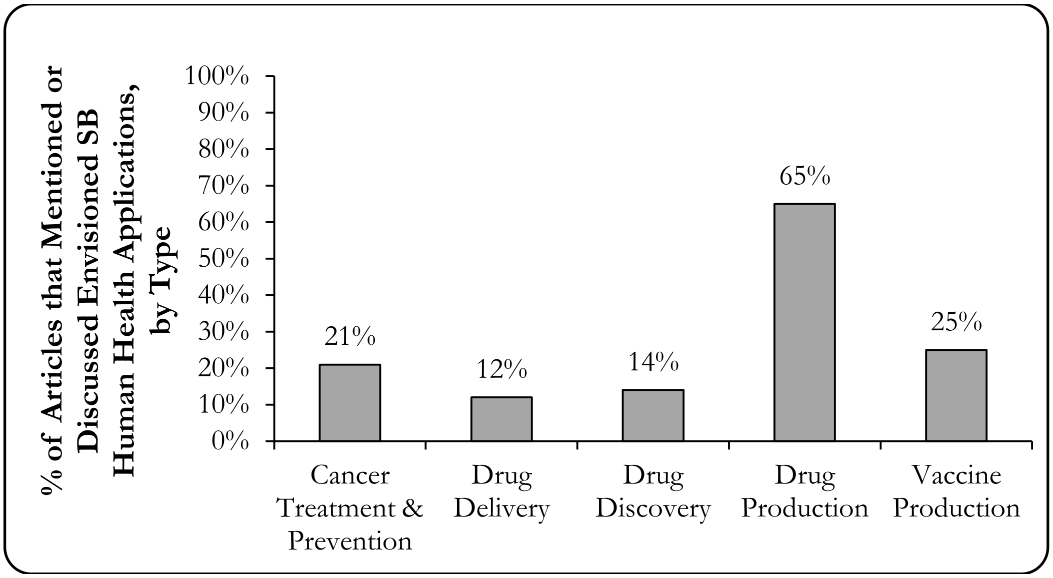

FIGURE 6. 7 PERCENTAGE OF ARTICLES THAT MENTIONED OR DISCUSSED SPECIFIC SB HUMAN HEALTH APPLICATIONS, BY TYPE

A broad range of envisioned human health products were identified during the scoping exercise, all of which can be categorized within at least one of the five application groups shown in Figure 6.7. In Table 6.7 (as follows), however, they have been organized into three different groups based on the *manner in which they could be used*:

1) Products that **produce a chemical** or **other therapeutic substance** (either *in vivo* or *ex vivo*)
2) Products that **act therapeutically within the body,** either as a sensor or mechanically
3) Products that **act therapeutically,** and **produce a chemical** or **other therapeutic substance, in the body**

and sub-classified based on their *therapeutic objective*: **1)** prevention, **2)** prevention and/or treatment, and **3)** treatment alone.

TABLE 6. 7 ENVISIONED SB HUMAN HEALTH PRODUCTS, BY THERAPEUTIC OBJECTIVE*

Produce a Medicinal Chemical or **Other Therapeutic Substance**	**Act Therapeutically within the Body**	**Act Therapeutically,** and **Produce a Medicinal Chemical** or **Other Therapeutic Substance, in the Body**
	Objective: Prevention	
• Viral and DNA-based Vaccines **(n=64)**	• Microbes Designed to Enhance the Function of our Immune System, Act More Efficiently **(n=5)** • Detection and Neutralization of Toxins (Primarily in Water) **(n=7)**	N/A
	Objective: Prevention and/or Treatment	
• Production of Designer 'Protein Drugs' such as Therapeutic Monoclonal Antibodies **(n=6)**	• Treating Genetic Disorders: Gene Therapy and RNA Silencing (anti-sense and RNAi)- using Nucleic Acid Drugs and Personalized Medicine **(n=16)** • Robot Surgeons: Microbes that Circulate within our Body and Detect and Treat Disease **(n=6)**	• Detecting and Treating Viral Infections, especially HIV **(n=8)** • Cancer Treatment: Locating and Killing Tumours **(n=53)** • Microbes Engineered to Detect and Dissolve Dangerous Substances that Accumulate our Bodies **(n=1)**
	Objective: Treatment	
Re-designed microbes that produce: o 'Natural' Pharmaceutical Products **(n=4)** o Antibiotics **(n=14)** o An Inexpensive Blood Substitute **(n=2)** • The Creation of Replacement Organs; Tissue Engineering & Regenerative Medicine **(n=21)**	• Bacteria and Bacteriophage Drug Delivery Systems & 'Smart Drugs' **(n=16)** • Microbes that Penetrate Biofilms **(n=2)**	• Devices that Analyze the Intercellular State Prior to Delivering a Therapeutic Effect (Controlled Delivery) **(n=1)** • Internal Biosensing Devices that Recognize when a Drug is Administered **(n=1)** • Type I, II Diabetes Treatment/ Management: Automatic Creation of Beta Cells and Cells that Monitor Insulin Levels **(n=7)**

* References for associated products can be found in Appendix B.4

Additional details about the therapeutic nature of the products described in Table 6.7 are found in Appendix B.4.

Throughout the scoping process, this author identified a number of documents that advocated for the implementation of SB in the human health sector. In the section that follows, the major points that arose from this discourse are addressed.

Advocating for 'synthetic' human health products

According to some, human health is an area wherein SB is destined to make "significant progress" (108). Indeed, the discipline could someday help scientists find treatments for a wide-range of complex diseases that currently "plague humanity" (329). Others assert the discipline will significantly improve our ability to maintain, and augment, human health (108,330).

Several documents portrayed SB as a discipline that would someday out-compete conventional techniques used to produce pharmaceuticals (203,331,332). As summarized in Table 6.8 (follows), this author identified demographics, economics, and time as the three main motivations behind the need to create SB-based pharmaceuticals.

TABLE 6. 8 THREE MAIN MOTIVATIONS BEHIND THE PRODUCTION OF SB-BASED PHARMACEUTICALS

Motivation	Explanation
Demographics	
Urbanization (n=1) (304)	• Infectious diseases rates have risen over the years; some have attributed to an increasing global trend toward urbanization o Growing number of infectious diseases comes the need for an increasing number of novel therapies

Aging Population (n=1) (304)	• The human population is aging; a trend especially prominent in developed countries
	  o By the year 2050, 20% of the world population will be 60 years old or more
	  o Demographic shift expected to cause increased need to devote economic resources toward health care for the aged; SB could prove valuable tools to help keep this aging population healthy

Economics	
Cost of Developing Drugs using Conventional Methods (n=7) (63,87,197,297, 332-334)	• Inability to produce complex and rare chemicals using conventional technologies: key motivations for SB • SB could reduce economic strain on pharmaceutical companies o Designer microbes that can created to produce rare chemicals instead of having to extract and purify them from plants
Employment Opportunities (n=1) (153)	• SB activities related to pharmaceutical development could lead to an increased number of jobs
Time	

Shorten the Time needed to Create Therapeutic Chemicals (n=8) (131,233,330, 335-339)	• It can take "hundreds of person-years of effort" to produce important therapeutic chemicals
	  o SB techniques could be used to speed up the production of vaccines
	  o SB might be especially useful in creating viruses that evolve quickly (*e.g.* HIV, common cold) - they can render many conventionally produced vaccines unusable quite quickly

Referred to as the "raison d'être" (332), "poster child" (340,341), and "most successful" (342) application of SB to date, the creation of 'semi-synthetic' Artemisinin using re-designed microbes was the most widely discussed pharmaceutical-based SB product vision across the documents examined. Indeed, of all the articles scoped in this study, more than one quarter (n=95 or 26%) mentioned or discussed this envisioned product in some detail.

The discourse surrounding SB's future in the human health sector was generally positive; however, some documents presented more sceptical views. SB's potential role in the treatment of genetic diseases and the development of vaccines were particularly questioned (52,153,343-345). With regard to vaccine production, one article noted that SB's DNA-based vaccines may "prove no more efficient or effective than [those produced using] conventional... techniques" (153,153). Another referred to SB's future in this area as "particularly uncertain" (345). Further, two documents (49,52) noted that SB future in the treatment of complex genetic diseases with **a)** no clear gene component and **b)** a large number of genes would prove particularly difficult.

Envisioned Veterinary Health Applications

Compared to envisioned human health products, envisioned SB veterinary health applications were scantly discussed across the literature examined. Indeed, only one percent of articles (n=5) (87,151,203,304,346) discussed SB's potential role within this sector. Of those articles, two (151,346) mentioned that SB might someday play an important role in animal health, and three (87,203,304) briefly mentioned the discipline's future potential role in the production of animal vaccines and related diagnostics. These products were only identified in reports.

Envisioned Industrial Applications

"Living Chemistry" (347)

In this study, products related to the industrial-scale production of materials (textiles, fabrics, polymers, and rubber) and non-pharmaceutical chemicals were the third most frequently discussed SB product vision. Of all articles examined in during the scoping exercise, 42% (n=154) either mentioned, or discussed, at least one envisioned SB industrial product. As illustrated in Figure 6.8, across all document types, reports discussed this sort of envisioned application more frequently than any other article type (92%).

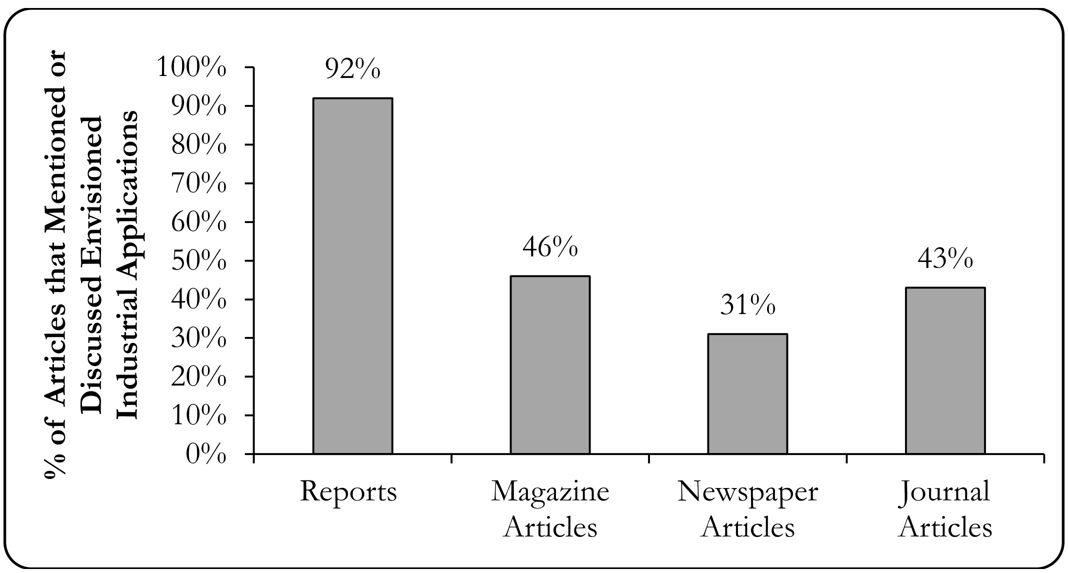

FIGURE 6. 8 PERCENTAGE OF ARTICLES THAT MENTIONED OR DISCUSSED ENVISIONED SB INDUSTRY APPLICATIONS, BY TYPE

The envisioned industrial products identified during the scoping process have been categorized into two main types based on the end product they produce: materials and non-pharmaceutical chemicals (Table 6.9).

Table 6. 9 Envisioned SB industrial applications

Type of Product	Details
Materials	
Plastics (n=37) *E.g.*(28,87,183,197, 316,348-350)	• With SB, it may be possible to manufacture the starting materials needed to produce plastics using microbes instead of relying on 'dirty' fossil fuels • This process could reduce the environmental footprint of plastics manufacturing and the synthetic production of L-lactate (major chemical components of bio-degradable plastic)
Textiles and Fabrics (n=8) (108,198,297,332, 351-353)	• Using SB, novel and designer materials could be woven into a variety of textiles and fabrics (*e.g.* silk and spandex)

Spider Silk
(n=15)
(28,48,104,108, 130,151,197,198, 351,352,354-358)
	• Industrial-scale manufacturing of 'spider silk' (protein-based fibre produced by the Golden Orb spider) a key target for industrial SB
	  o World's strongest known natural fibre (10x stronger than Kevlar)
	  o Could be manufactured industrially using SB techniques, for a variety of applications: medicine (*e.g.* plastic surgery) to defence (super light body armour)

Natural Rubber (n=1) (332)	• Synthetic rubber has been produced for hundreds of years in the laboratory settings, SB could be used to design specialized 'natural' rubber-producing bacteria
Non-Pharmaceutical Chemicals	

Chemicals in General
(n=102)
E.g.(87,201,304,306, 316,332,333, 359-361)
	• SB-based production of chemicals: several advantages over conventional synthetic methods.
	  o SB production methods are anticipated to be more a) environmentally friendly, b) economically feasible, c) efficient and d) simple
	  o "promise to simplify and expedite" (359) the conversion of a variety of feedstocks into useful chemicals

1,3 propanediol (PDO)
(n=19)
(28,89,183,297, 304,310,314,324, 343,344,348,353, 362-368)
	• Chemical manufacturer DuPont and biotechnology company Genecor (now owned by DuPont) successfully engineered *E. coli* to produce 1,3 propanediol (PDO)
	  o Chemical is an important component of a spandex-like fibre called Sorona
	  o Can be turned into a variety of different textiles such as carpet fibres
	  o SB produced PDO could become the "first $1 billion biotech product that is not a pharmaceutical"

Many documents emphasized the *economic* benefits that could be gained if SB became successful in this application area. In the section that follows, key points related to this discussion are presented.

The economic benefits of 'synthetic' chemical production

According to the Organization for Economic Co-operation and Development, at least until the year 2015, the industrial production of chemicals using metabolically-engineered microorganisms could become the most viable commercial application of SB (151). Other organizations are just as optimistic about SB's future in the industrial production of chemicals. A 2009 Concept Note by Lowrie & Tait (131) suggested that, along with energy-related products, the profits from SB-based chemical production could reach $1.6 million by the year 2013. Further, a 2010 report by the Presidential Commission for the Study of Bioethical Issues asserted that the SB chemical industry alone "could generate global revenue of $1 trillion", although no timeline for this prediction was provided (153).

In order for the economic predictions described above to have any hope of becoming reality, several obstacles will first have to be overcome. SB-based industrial products will have to be produced at a) higher quality, at an b) equal or larger scale and c) for less money than traditional chemical production methods (303,362). Indeed, according to one document, in order for new biotechnological production methods to become worthwhile, they have to "reduce costs by 30%" (362).

Envisioned Environmental Applications

A total of n=111 (30%) articles reviewed mentioned, or discussed in some detail, a variety of envisioned SB products that could someday present a variety of benefits for the environment. For example, SB could be used to produce alternative sources of energy that might someday reduce our carbon footprint. Here, the discussion is limited to envisioned products that act *directly* upon the environment to **detect and monitor** hazardous chemicals and/or **assemble**, **degrade, or treat** those substances.

While less than half of all magazine, newspaper, and journal articles reviewed mentioned or discussed SB-related environmental products, nearly all (24/26) reports did (Figure 6.9).

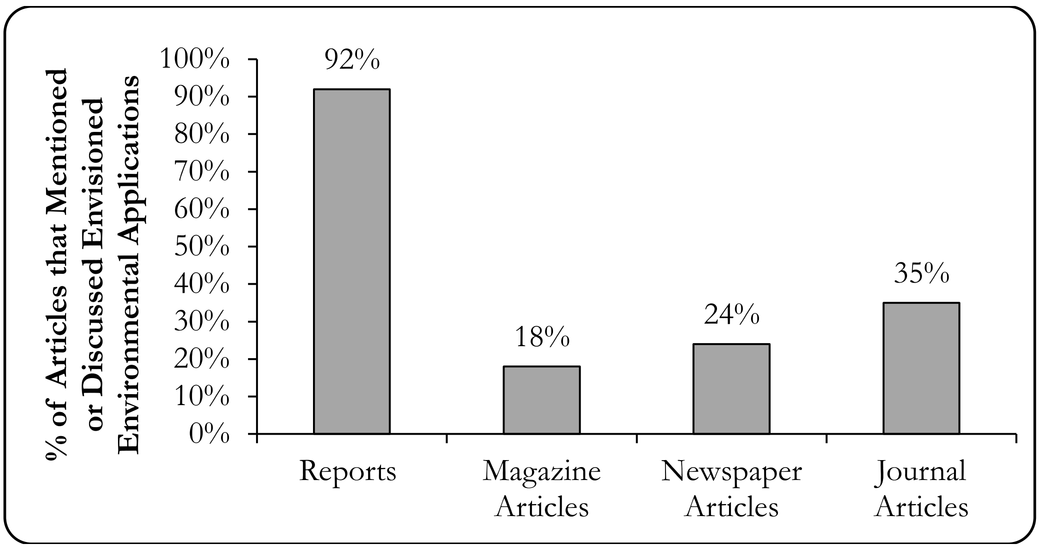

FIGURE 6. 9 PERCENTAGE OF ARTICLES THAT MENTIONED OR DISCUSSED ENVISIONED ENVIRONMENTAL APPLICATIONS, BY TYPE

A breakdown of relevant products identified during the scoping exercise is provided in Table 6.10 (follows). Briefly, products were categorized into one of two main types: **1)** environmental bio-sensors and **2)** products designed to monitor, detect, and/or degrade pollutants.

TABLE 6. 10 ENVISIONED SB ENVIRONMENTAL APPLICATIONS

Envisioned Application	Details
Environmental Bio-sensors	

Cellular Bio-sensors (n=6) (52,130,319,320, 369,370)	• Cells could someday be engineered to:
	  o Sense and monitor air, soil, and water quality
	  o Those capable of recognizing a target pollutant(s) with high sensitivity, whilst producing a real-time measureable output are expected to be especially desirable
	• A completely self-sustainable and self-reproducing bio-sensor that could be left in the field to continuously monitor environmental conditions is also desirable

Environmental Monitoring, Detection, and/or Degradation of Pollutants	
Plant Bio-sensors (Phyto-detectors) (n=1) (371)	• Plants: o Generally ubiquitous, do not require a great deal of maintenance, have the natural ability to "sense and respond to their environment" (371) • SB could be used to modify or enhance plant traits to create highly specialized phyto-detectors

Bio-remediation (n=94) *E.g.* (88,119,200,233, 304,369,372-379)	• Microbes could be created to metabolize environmental pollutants that are resistant to natural degradation
	• There are several types pollutants that SB engineered microbes might someday be able to accumulate and/or remove in an economical, efficient, and safe manner:
	  o polychlorinated biphenyls (PCBs)
	  o industrial coolants and solvents,
	  o nuclear waste from energy production facilities,
	  o heavy metals, and
	  o hydrocarbons, either from oil spills or toxic bi-products released from burning transportation fuel, tar, and coal

Envisioned Food Applications

Food-related applications were the fifth most frequently identified type of envisioned SB product with a total of n=39 (11%) of articles having either mentioned or discussed applications within this domain. Across article types, a greater proportion of reports (n=9 or 35%) mentioned or discussed envisioned food applications than any other article type.

Table 6.11 (following page) shows two broad categories of food products identified: 1) the production and maintenance of food products and 2) products that relate to food safety, enhancement of food properties, in addition to the production of vitamins.

TABLE 6. 11 ENVISIONED SB FOOD APPLICATIONS

Product or Application	Details
Production and Maintenance of Food Products	

General (n=16) (49,153,201,310, 323,337,380-389)	• SB could be used to:
	  o increase meat production,
	  o modify algae to produce "artificial steaks" (323),
	  o create edible materials with built-in nutritional properties of foods (*e.g.* corn, beef, and fish)
	  o create new types of foods
	  o detect food spoilage

Flavours (n=8) (28,104,139,198, 304,314,362,365)	• Mass production of some flavours (*e.g.* strawberry) is expensive when the flavour is extracted and purified from a natural source. • SB could be used to create flavours more efficiently and economically

Food Sweeteners (n=2) (48,183)	• Using conventional methods, the large-scale production of artificial food sweeteners (*e.g.* xylitol and L-alanine, saccharin) can be expensive
	  o SB techniques could be used to produce these sweeteners in a more efficient and economical manner
	• Using SB, soy plants and/or microbes, could be modified to produce glycyrrhizin (odourless compound in liquorice root), which is several times sweeter than table sugar.
	  o Production of liquorice could be re-located from Far and Middle Eastern countries to the laboratories and/or soybean fields of Western countries

Food Ingredients (n=4) (48,88,108,336)	• SB could bring new biology-based production techniques for important food ingredients • SB could be used to synthetically produce food oils (including tropical oil substitutes)
Food Safety, Enhancing Food Properties, and Vitamin Production	
Food Processing (n=1) (390)	• Bacteriophage could be engineered to attack dangerous Biofilms in food processing settings
Enhancement of Food Properties (n=2) (151,391)	• SB could be used to prolong shelf life of vegetables and fruits; could also be used to 'waterproof' bananas so that they remain ripe for months
Vitamin Production (n=12) (28,53,108,151,344, 351,353,364,392-394)	• Worldwide, thousands of people experience Vitamin A deficiency, which can cause widespread blindness and even death • *E.coli* could be re-engineered to create Vitamin A, a process that could result in a more economically-stable production method than that which is currently used

Envisioned Agriculture Applications

As the sixth most frequently discussed application area, approximately one in ten documents (n=35) analyzed in this review either mentioned, or discussed, envisioned SB agriculture applications in various amounts of detail. While 16/26 (62%) of reports reviewed in this study mentioned at least one envisioned SB product related to this application area, comparatively few of the journal (9%), magazine (7%), and newspaper articles (3%) reviewed in this study did.

As described in Table 6.12 (follows), the agricultural applications identified during the scoping process mainly related to the modification or enhancement of crops (Table 6.12).

TABLE 6. 12 ENVISIONED SB AGRICULTURE APPLICATIONS

Product or Application	Details
General Agricultural Applications	
Envision SB Playing a Role in Agriculture (n=18) (28,48,104,128, 151,153,169,203, 254,314,319,351, 356,357,395-398)	SB could be used to: • dramatically change traditional approaches to agricultural biotechnology • create more affordable agricultural products • help increase global food security
Crop Applications	
Combat Biofilms (n=1) (390)	• Specialized bacteriophage (viruses that attack bacteria) could be created to attack dangerous agricultural biofilms (*e.g.* biofilm diseases of agricultural crops)
Novel Crops, Crop Modification & Enhancement (n=21) (48,83,104,108, 151,153,203,232, 255,295,297,304, 310,314,358,371, 399-403)	SB could enable the creation of: • entirely new crops • seeds that are resistant to pesticides • crops that produce their own insecticide and fertilizer that can also be used by subsequent years' crops Using SB, crops could be synthetically engineered to become: • Salt , heat, and drought resistant and/or tolerant • Higher-yielding • Super-efficient (engineered to use non-natural methods of nutrient uptake, *e.g.* plants that nitrogen-fix) • Disease, pest, and pesticide resistant • Optimized for 1) oil production (oilseed crops), 2) use in bio-fuel applications, 3) numerous nutritional benefits (*e.g.* higher protein levels), and 4) tolerating challenging environmental conditions
Nutrient Monitoring (n=1) (153)	• Biological sensors could be created to monitor soil for nutrient quality and/or detect environmental degradation

Envisioned Defence Applications

Two types of envisioned SB-based 'military' applications were identified during the scoping process: 'negative' applications, such as the creation of designer bio-weapons for the purposes of bio-terrorism (see emergent themes, sub-section 6.1.3), and 'positive' applications, such as SB products created to protect citizens against military threats (345). Here, discussion is limited to the ‘positive’ military applications identified during the scoping process, collectively referred to as ‘bio-defence’ applications.

Biological defence applications were not discussed as frequently as ‘negative’ military applications (7% compared to 29% of articles reviewed), though this author noted a specific particular sense of enthusiasm about SB future in this domain. Indeed, the United States Department of Defence, for example, has already established a ‘Task Force on Military Applications of Synthetic Biology’ through which it aims to study ways in which the discipline could someday be applied to develop novel defence technologies (233,404).

Of the n=25 documents that mentioned or discussed at least one envisioned bio-defence application, most (n=12) were reports. This type of envisioned SB application was discussed second most frequently in journal articles (n=6), followed by articles published in magazines (n=4), then newspapers (n=3). Once identified, these applications were categorized into three main types: biological sensors, bio-defence tools, and model organisms (Table 6.13).

TABLE 6. 13 ENVISIONED SB DEFENCE APPLICATIONS

Product or Application	Details
Biological Sensing	
Using SB in Biological Defence Applications (n=9) (87,88,139,153, 232,254,395,404,405)	• SB could someday be used to create several types of defences against bio-terrorism and bio-warfare, and other bio-security risks
Bacteria-based Bio-sensors (n=2) (345,369)	• Specialized organisms could be designed to identify biological hazards, such as pathogenic organisms o These organisms would be most useful if engineered to have a focused effect on hazards, have no harmful effect on benign organisms
Sensing Various Chemical Targets (n=12) (48,108,200,304, 319,344,346,369, 370,406-408)	• Detecting, Monitoring, and/or Neutralizing: o Landminds (*e.g* detection of 2-4-dinitrotoluene, commonly associated with landmines), & o Chemical agents (*e.g.* nerve gas) and explosives (*e.g.* Trinitrotoluene (TNT)), o Biological agents (*e.g.* airborne pathogens)
Bio-defence 'Tools'	
Vaccine Development (n=3) (345,409,410)	• SB could be used to create vaccines to combat man-made biological threats
Model Organisms	
Plant-based Bio-sensors (Phyotdetectors) (n=2) (371,408)	• Plants "naturally sense and respond to their environment" (408), would require low maintenance, and are largely ubiquitous. This makes them ideal organisms to detect landmines

Envisioned Science Fiction/Fantasy Applications

This author differentiated SB-based products identified during the scoping process as 'science fiction/fantasy' if they appeared to this author as **a)** implausible, but possible, in the real world under certain circumstances, or **b)** virtually impossible in the real world under any condition. In the end, only 4% of the documents examined (n=15) mentioned products of this nature making this application area, making it the least frequently discussed of all other application types. Further, compared to all other types of documents analyzed, more magazine articles (n=7) mentioned or discussed SB products of this nature than any other type.

This author identified a variety of SB fiction/fantasy applications during the literature scoping process, from the creation, modification, enhancement, and control of humans and other non-human animals to the design and creation of novel microbes capable of creating numerous types of inanimate objects (Table 6.14).

TABLE 6. 14 ENVISIONED SB SCIENCE FICTION/FANTASY APPLICATIONS

Application Category	Envisioned Product or Application
Humans	
Creation, Modification, & Enhancement (n=10) (48,233,254,380, 381,400,405, 411-413)	• SB could be used to create: o foetuses solely to harvest parts o designer children (or clone them) o humans or human-animal hybrids • The discipline could also be used to: o engineer novel human traits; augment those that already exist, o modify higher forms of life o build 'biological computers' that circulate and replicate throughout the cells in our body o transform the human body into astonishing new forms, or even o Engineer hyper- aggressivity genes in embryos to create "fearless soldiers" (405)
Animals (Domestic, Extinct, Livestock)	
Creation & Modification (n=7) (101,254,352,399, 400,412)	• Made-to order pets • Create creatures similar to dinosaurs • Re-create mammoths and Neanderthals • Engineer o novel types of livestock, o pigs with wings, and o cattle to produce human milk for use as infant formula
Plants	
Creation & Modification (n=2) (378,400)	• Engineer flowers to bloom on command • Create novel types of plants
Microbes & Insects	
Creation (n=2) (400,414)	• Create novel microbes that produce a supply of a specific desired food product (*e.g.* egg nog) • Custom-made insects that "seek out and kill locusts or malarial mosquitoes" (400)
Inanimate Objects	
Creation (n=4) (28,325,378,415)	• Re-program a tree genome(s) with the ability to grow: o a table, o bookshelf, o bridge, o house, and o other 'mega-structures'

In addition to the products described in Table 6.14, this author identified several documents that described "the alpha Synthusiast" (412) Drew Endy's SB's product fantasies (n=6). Quotations describing each of Endy's product fantasies have been summarized in Table 6.15[24], directly as follows.

TABLE 6. 15 DREW ENDY'S SB PRODUCT FANTASIES

Drew Endy's SB Product Fantasy	Supporting Quotation
Re-programming trees to:	
Grow into houses	"One of Endy's long term ambitions is to re-design the seeds of a tree such that the tree is programmed to grow into a house" (28)
Grow into a mega-structure	"We should be able to combine redwood and bamboo to quickly grow a mega-structure" (378)
Grow a bridge	"I'm a structural engineer- I get to retire when I can grow my own bridge". "It is a fun fantasy, but if I could enable that, that would be cool" (378)
Grow a bookshelf	"You could program the DNA in the tree so that it grows into a bookshelf" (325)
Designing and engineering life forms, and life-like creatures from scratch, including:	
Children	"Endy stopped long enough for me to digest the fact that he was talking about building our own children" (412)
Artificial versions of various organisms	"If you can sequence something properly and you possess the information for describing that organism--whether it's a virus, a dinosaur, or a human being--you will eventually be able to construct an artificial version of it" (412)

The findings related to envisioned SB products differentiated by application area have now been concluded. As mentioned previously, during the scoping process, this author identified several 'timeline' predictions pertaining to *when* SB's product visions might someday become realized. What follows is a brief exploration of these findings.

Timeline to SB Product Realization

At the present time, most SB products remain in a preliminary of research and development phase and are predicted to be many years away from becoming realized (104,153,416). Just like all emerging technologies, however, the pace of development could be

[24] Dr. Endy contributed to the development of a science comic titled "Adventures in Synthetic Biology", published in Nature's 2005 special issue on SB.

hastened by breakthroughs that were not foreseen, emphasizing the unpredictability of the pace of discovery (153,203). Toward this end, this author identified several short and long term 'timeline' to realization predictions that were made about SB's products during the data analysis process. Table 6.16, as follows, presents a summary of those predictions.

TABLE 6. 16 SHORT AND LONG-TERM TIMELINE TO REALIZATION PREDICTIONS FOR ENVISIONED SB PRODUCTS

Short-Term Predictions	Long-Term Predictions
Well understood naturally-occurring organisms will be synthetically engineered. These organisms will be used to produce various industrial chemicals (343)	The complete synthesis of novel living systems that do not exist in nature (protocells). These organisms will be used for wider applications, beyond the production of various industrial chemicals (130,417,418)
SB's *increasing presence in*: • Production of bio-fuels (153), • various industrial chemicals, • influenza vaccine production (383) • agricultural applications, especially the genetic modification of plants and other organisms for the purpose of food production (151)	SB's *widespread use as a*: • "primary" method used in industrial manufacturing, • medicine (151), and • environmental applications (especially bioremediation) (130)

Whereas long-term SB timeline predictions include the creation of novel protocells for use in wide range of application areas, short term predictions mainly involve what could be considered a simple extension of genetic engineering (52,131).

6.1.3 EMERGENT THEMES

While immersed in the data synthesis process, this author identified six broad-reaching themes that emerged from an analysis of envisioned SB product discourse. These have been broadly differentiated into the following groups: 1) 'Selling' Synthetic Biology, 2) Metaphorically Speaking, 3) Science Fiction and Frankenstein, 4) Improving and Enhancing Nature, 5) The Social Risks and Concerns of Synthetic Biology, and 6) Downplaying Synthetic

Biology's Risks and Concerns. In the sections that follow, the findings that emerged within each of these themes are explored.

'Selling' Synthetic Biology

While immersed in the data, this author noted an overall sense of promise, excitement, and amazement conveyed about the benefits SB and its "countless" number of envisioned products could one day bring society (89,324,325,348,356, 373,399,415,419,420). According to some, the discipline could positively "influence almost every aspect of human life" (348) and carries with it a "staggering potential" to benefit society (89). Overall, this author noted the emerging field was generally 'sold' as a discipline so potentially valuable that society *must* allow its continued development.

The literature placed special emphasis on the potential SB could bring to the fields of medicine, agriculture and industry. Several other documents (43,52,378) noted the discipline could even play a broader role in the emergence of a second industrial, or a third technological, revolution (43,52,378). As part of this revolution, SB was described as a field destined to produce numerous practical applications in order to a) fulfill several market needs (303,360,421) and b) resolve the world's most pressing societal challenges (299,400,419,422-424).

During the data synthesis process, this author noted SB practitioners' were generally portrayed as scientists conducting innovative research in order to address humanitarian concerns. Indeed, the data revealed that SB practitioners' desire to conduct their research was not simply based on a desire to *address* "real world" social problems, but rather, to *solve* them (28,52,63,89,197,233,254,336,344,351,362,379,423,425,426). Some of the most frequently cited societal challenges on SB's target: the growing and aging population (human health crisis), decreasing crop yields (food security issues), energy shortages (the energy crisis), water shortages (52,153,295), and increasing environmental damage (climate change crisis) (254,295, 388,400,427,427). Through the development and commercialization of numerous 'practical' SB applications to address those needs, the discipline was described as society's only hope for an imminently dark future.

Metaphorically Speaking

During the data analysis process, this author noted four re-occurring metaphors frequently associated with envisioned SB product discourse: 'science fiction' and 'Frankenstein' in addition to the religious metaphors "holy grail" and "playing God". The use of the term 'science fiction' and 'Frankenstein' will be described first, followed by a description of the religious metaphors 'holy grail' and 'playing God'.

Science fiction and Frankenstein

While immersed in the data, this researcher noted the re-occurring theme of SB, and its potential products, having been described within the context of science fiction (48,325,411,413,428,429). Some documents described SB's current research aspirations such as "genetic tinkering" and the creation of an entirely synthetic organism as 'science fiction' (104,326,430). Others emphasized that, with the help of SB, products that once might have seemed 'extra-terrestrial' are closer than ever to becoming reality (351). This notion was further emphasized by Weintraub (323) who asserted that "twenty years from now, the things [synthetic biologists] are doing now will look frighteningly primitive".

Complementary to the theme of science fiction, this author noted the frequent use of the term 'Frankenstein' in conjunction with SB envisioned product discourse. Indeed, just as the discipline's research, and its envisioned products can bring to mind images of science fiction, they might also evoke images of synthetic biologists playing the role of 'Dr. Frankenstein' (431). While some documents appeared to legitimize its use as a metaphor for SB research, several others discouraged the comparison, deeming it grossly inappropriate (128,372,385, 411,432,433). For example, a 2010 newspaper article published in the Toronto Star (434) noted that creating a protocell is far different, and far less complicated, than attempting to create higher organisms- especially human beings. Indeed, Dr. Frankenstein sought to create a human being whereas synthetic biologists seek to create "planned [minimal] organisms" (341) that might someday provide society with much needed alternative fuels and vaccines (434).

Religious metaphors: 'Holy Grail' and 'Playing God'

Especially since the successful creation and transplantation of the first completely synthetic microbial genome in 2010 (see sub-section 2.4.3), synthetic biologists have been accused of 'playing God' (151,435). Across literature that appeared to be particularly critical of SB, this author noted the metaphor was generally used to describe ill-intentioned research on the part of "arrogant" synthetic biologists (151,434-436). According to some of these documents, when scientists pretend to be God, they could become misled by "the power of sin" (436) - a risk that could ultimately cause the world's great demise (389).

Across the literature that appeared particularly supportive of the discipline, this author noted a generally defensive attitude toward the accusation that SB practitioners 'play God'. A 2010 comment published in the Guardian newspaper, for example, noted that humans have been 'playing God' for centuries (385). Indeed, the aims of SB practitioners are no different than the intentions of humans during the invention of agriculture and emergence of domesticated animals (385). Practitioners are focused on creating *practical* applications for the benefit of humanity, and thus, they have no desire to 'play God' (437).

Holy Grail

The term 'Holy Grail' was frequently used to describe a variety of envisioned SB products predicted to 'revolutionize' the field. At least two documents referred to energy production as the Holy Grail of SB (254). Other products dubbed SB's 'Holy Grail' included self-sustained environmental bio-sensors and microbes built to eliminate toxic waste (320,344).

Improving and Enhancing Nature

While immersed in the data, this author noted the emergence of a predominant theme that SB not only can, but should, be used to improve the 'inadequacies' of nature (57). According to at least some SB practitioners, the only way to adequately address today's major societal issues is to re-engineer naturally occurring organisms, or create custom-made living machines, with superior traits that can *out-compete* their natural counterparts (254,299,373, 400,438). Indeed, if society viewed nature as a machine, they would "see that it is not perfect and that it can be revised and improved" (52). This theme emerged within the context of human health as well. Indeed, at least five documents (201,233,357,388,439) discussed the possibility of using SB to augment, improve, and enhance human physical health.

The 'Social' Risks and Concerns of Synthetic Biology

The breadth of potential benefits SB could someday offer society is reflected in the numerous envisioned products identified during the scoping process (sub-section 6.1.2). This discussion emerged, however, in parallel with a substantial amount of discourse surrounding the risks and broad societal concerns those products might someday bring society. Indeed, of all articles analyzed in the scoping review, this author noted that slightly more than half (52%

or n=190) mentioned at least one risk or societal concern associated with an envisioned SB product(s) (Table B.7).

The SB product risk discourse identified during data analysis was differentiated into two broad types: the a) **physical risks** of envisioned products, including their bio-security, bio-safety, and environmental risks, and b) **non-physical concerns** associated with ethical and intellectual property (42,344,440). These risks and concerns are interlinked, and thus, it is inherently difficult to separate discussion around each of these risks into distinct categories. Nevertheless, this author has attempted to differentiate between the discourse that emerged surrounding each of the risks and concerns in the sections that follow.

Bio-security risks

Two products created using SB techniques exemplify its bio-security risks: the successful re-creation of the *1918 influenza* and highly infectious *polio virus* using **a)** genetic sequences derived from a victim frozen in permafrost and **b)** mail-ordered segments of DNA (417,441). Indeed, at least two documents asserted these events have already made "the work of bioweaponeers" much easier; they could even change the way countries engage in war (28,441). It was within this context that the majority of SB product risk discourse emerged, as discussed in further detail in the paragraphs that follow.

SB's potential to create new and more powerful weapons for the purpose of bio-warfare and/or bio-terrorism was mentioned or discussed in 29% (n=108) of the articles examined. Within this context, the literature explained that "maverick scientists or terrorist groups" (442) could someday use SB techniques to **1)** create harmful organisms that are more virulent than any disease currently known and/or **2)** modify existing pathogens, such as Ebola, and Smallpox with features that would make them even more virulent (443,444).

Within the context of SB and bio-terrorism, this researcher noted the emergence of two prominent risks across the literature examined: **1)** engineering microbes with a built-in resistance to antibiotics (n=9) and the **2)** 'dual-use dilemma' (n=27). Briefly, the 'dual use' concern refers to research on pathogens, smart drugs, and/or viral vectors originally intended for 'good' that can be easily diverted to create harmful agents (52,93,106,106,153,345,399,445). Indeed, the DIY Bio movement (sub-section 2.6.3) has continued to fuel concerns over the possibility for misusing the discipline in this capacity as members currently pursue unregulated experiments in the 'safety' of their own home (254).

While many articles focused on SB's bio-security risks themselves, several documents also discussed ways in which those risks could be mitigated. For example, Balmer & Martin (139) suggested the establishment of a robust regulatory framework *before* SB's applications become realized. This oversight framework might include restrictions on access to materials with dial-use properties, or a licensing and registering control on tools used in SB research (48,87,153). Further suggestions for mitigating SB's bio-security risks included **1)** the need for companies to screen orders for synthetic DNA against the sequences for known pathogens and **2)** the creation of a professional SB society requiring all SB practitioners to obtain membership (108).

Bio-safety risks

The most widely discussed bio-safety risk identified by this author was the potential for synthetic organisms to accidentally escape from the laboratory (n=28, or 8% of documents). Another less frequently identified bio-safety risk related to the inadvertent infection of laboratory staff by un-natural microbes (87) (Appendix B.8). These issues elicited questions around the most appropriate level of laboratory containment in which SB research is conducted (28). This author noted at least four articles that suggested SB research should not be conducted in university laboratories given their relatively low level of security (289,442,446,447). These documents generally argued that the lower the level of laboratory security, the greater the chance that an “artificial” organism might unintentionally escape and could potentially cause irreversible harm to the natural environment (289,442,446,447).

Environmental risks

While immersed in the data, this author identified a prominent environmental risk that emerged within the context of SB product discourse: if novel organisms were somehow able to reach the open environment- deliberately or accidentally- they could indeed create new forms of “living pollution” (48,52,93,104,255,314,331). Indeed, genetic information from artificial organisms could conceivably transfer to natural organisms, which could disrupt the delicate balance of natural ecosystems and might even result in the creation of novel diseases.

During the data synthesis process, this author also identified three main ways in which SB practitioners believe their products’ environmental risks could be mitigated. First, a ban could be placed on the use of synthetic organisms outside the confines of a laboratory, at least until sufficient risk assessments can be conducted to ensure organisms in question are ‘safe’ (52,108). Second, synthetic life could be designed with built-in “suicide”, “kill switch”, or “fail fast” genes (130,153,254,447). Similarly, synthetic microbes could also be created without the genes required to manufacture key chemicals they require to live, such as amino acids (404). Without a steady supply of the missing chemical, the organism would not survive. Third, synthetic organisms could be created using un-natural DNA. Theoretically, this action would make organisms incompatible with natural flora, preventing genetic contamination (104,151).

Many SB practitioners believe the "safety-by-design" (379) practices previously described would "guarantee absolute containment" (448) and provide them with maximal control over the synthetic organisms they create. While those sentiments appeared to dominate the literature examined, this author also identified information that contradicted those assertions (254,314,379). A 2010 report by Friends of the Earth, for example, held that scientists "cannot just engineer safety into synthetic organisms" (254). A 2010 report by the ETC group (314) emphasized this point by describing the unforeseen environmental issues that emerged with the use of transgenic crops in the 1990's (314). When transgenic crops were approved for use in the open environment, many assumed that that they would be "too weak to outcross with conventional crops" (314). In reality, this assumption was proven false: today, low levels of genetic contamination are detectable in corn, canola, and cotton crops (314).

Intellectual property concerns

Today, a great deal of SB research is completed within the confines of a widely established open source movement (139). Although this movement dominates, over the past few years, the number of SB patent applications has increased (449). Perhaps the most controversial SB-related patent to date was J. Craig Venter's May 2007 application for a reduced version of the *M. genitalium* genome as discussed in sub-section 2.4.3 (62,108). If eventually granted the patent for this 'minimal bacterial genome', Venter stated his company would have restricted rights on the methods used to create synthetic organisms in over 100 countries (449)[25]. This author identified a number of concerns related to the ownership of life,

[25] Venter and his team anticipated potential opposition to the minimal genome and commissioned an ethics study by an independent panel of experts to investigate potential risks (87,531). The panel's 1999 publication concluded that, "the prospect of constructing minimal and new genomes **does not violate** any fundamental moral precepts or boundaries" (532).

many of which were fuelled by Venter's controversial patent. These concerns are explored in further detail as follows.

Several documents identified by this author suggested that Venter's patent could ultimately lead to the monopolization of key SB products such as fuel, chemical, and pharmaceutical-producing microbes (295,427,450). Such ownership could lead to the dangerous exploitation of future products based on self- as opposed to societal- interest (295,395,427). This author also identified several intellectual property regulations that might prevent Venter's research group from becoming the 'Microbesoft' of SB (52,139) Some argued the best option is a mix of both patent and open source options, but did not expand on details (52,139). Others still maintained that patents ought to be restricted to SB's *commercial* applications, such as re-engineered microbes that produce fuel and industrial chemicals (450). Whatever decisions are made concerning the discipline's intellectual property, SB practitioners insist that future patent regulations must not impede its advancement (139).

SB's intellectual property concerns cannot be entirely separated from its ethical concerns, especially those related to patenting the "essence of life itself" (108). In the section that follows, the ethical concerns that emerged during the data analysis process are explored in further detail.

Ethical concerns

This researcher identified a total of n=128 articles (35%) that mentioned or discussed, ethical concerns related to SB's envisioned products (Appendix B.8). The concept of artificiality, and SB practitioners taking on the role of 'creator', emerged as two of the most prominent ethical concerns identified by this author. Other concerns identified related to distributive justice*, i.e.,* whether or not the field's envisioned product benefits might someday reach *everyone* in need (131). The ethical implications of the semi-synthetic production of the anti-malarial drug Artemisinin also emerged as a predominant ethical concern across the literature analyzed (254,314). Whereas re-engineering yeast cells to produce synthetic Artemisinin might mean lower drug costs for individual patients, the process could devastate farmers of East Asia and Africa who farm the plant from which the chemical is currently extracted (314,451,452). Thus, while this action might benefit malaria patients, it might also harm the well-being of farmers in third world countries.

Downplaying Synthetic Biology's Risks and Concerns

Synthetic biologist J. Craig Venter once stated that he and his fellow SB practitioners "don't try to downplay" the risks associated with their discipline (323). While immersed in the data analysis process, however, this author identified evidence that does not necessarily support this statement. Indeed, this author identified at least six documents that put forward the notion that SB's risks are outweighed by its envisioned benefits (385,391,393,410,453,454). Within this context, some documents argued that every new technology has concerns and the potential for good or evil (404,455) . Indeed, with proper <u>foresight</u>, the risks and concerns associated with SB will someday become unfounded (128).

As noted by Khalil & Collins (197), society should instead focus its attention on "real threats" such as global warming, instead of "worrying about unlikely events" (456) commonly discussed in SB's risk discourse. Further, this author identified at least four articles (43,87,93,151) that downplayed the threat of bio-terrorism within the field. These documents described the notion of using SB to create specialized bio-terrorist agents as "extremely unlikely"- especially given the "major technical hurdles associated with weaponization and delivery" of micro-organisms (43,87,93,151).

6.2 ALBERTA-RELEVANT SYNTHETIC BIOLOGY PRODUCT IDENTIFIED

The exemplar product chosen to undergo this study's upstream product assessment was **synthetically re-engineered microbes that produce bio-butanol transportation fuel**. Indeed, numerous products identified during the scoping exercise might someday impact the lives of Albertans. In this study, the focus was limited to one of those products.

Table 6.17 (following page) presents the five criteria that were used to identify this Alberta-relevant product, and corresponding rationale for having chosen it.

TABLE 6. 17 CRITERIA, AND SUPPORTING RATIONALE, FOR THE EXEMPLAR PRODUCT CHOSEN FOR UPSTREAM ASSESSMENT

Criterion	Rationale
Public Support (214)	• A 2010 Alberta public opinion survey revealed that the majority of respondents were **supportive of using SB to produce bio-fuel** • Bio-fuels have the potential to reach, and benefit, **a wide number of Albertans**
Economic Structure (218,220,221,223, 230)	• Alberta considers advanced technology and innovation an **area of key importance to diversifying the province's economy** • Energy is Alberta's **main economic driver** • Given the province's experience and success in the energy industry, it could **become a leader in bio-fuel production and marketing** • Aside from the energy sector, agriculture and forestry also provide important contributions to Alberta's thriving economy. These **products could be used as feedstocks** for those microbes.
Political Landscape (229,230)	• For nearly eight decades, Alberta's government has remained **"staunchly pro-business"** (226) • Alberta has chosen to adopt the **'Renewable Fuels Standard',** requiring that at least five percent of gasoline used in 2010 be composed of renewable fuels by 2012
Research Investment & Innovation Priorities (146)	• Alberta Innovates: Energy and Environment Solutions was created to pursue **novel research in energy exploration**, the agency places special focus on "ecologically responsible energy" (146) and **renewable energy technologies.**
Alberta SB Research (108,212,213)	• 2007 Alberta-based iGEM team, the '**Butanerds**', won first place in the competition's Energy and Environment category for their bio-butanol producing *E.coli* microbes • **Current work University of Alberta's Bio-refining Conversions Network**: engineering *yeast*, not *E.coli,* to ferment provincially-grown sources of biomass and produce bio-butanol

Overall, Albertans' public opinion and the province's overall economic structure, political landscape, research investment and innovation priorities and its current and historical SB research are generally conducive to the emergence of the exemplar product. In the section that follows, the upstream product assessment framework that was developed to assess this product's potential implications on the social well-being of Albertans is described.

6.3 UPSTREAM PRODUCT ASSESSMENT (UPROD)

This study's upstream product assessment framework was comprised of two main dimensions. The first dimension consisted of three elements, each of which is described in Table 6.18 as follows.

TABLE 6. 18 THREE ELEMENTS COMPRISING THE UPROD FRAMEWORK'S FIRST DIMENSION

Element	Rationale
ACTION 1:	
Identify and explore the regulatory framework of an existing product or technology that is similar to the SB product of interest	Historical experiences from similar technologies can help guide the analysis process and could help identify potential oversight issues relevant to the product analyzed
ACTION 2:	
Identify a conventionally used counterpart to the SB product in question and the risks and benefits of replacing that counterpart with the SB product of interest	If a SB product is set to replace a conventionally used product, it should be at least as safe and offer as much benefit to society as the conventionally used product
ACTION 3:	
Identify stakeholders who might be impacted by the SB product of interest	Stakeholders will likely be impacted differently by the SB product of interest, and thus, the upstream assessment should focus on identifying potential implications on a stakeholder-specific manner

As shown in Table 6.18, the first dimension of UProd requires the assessor to perform three 'fact-finding' actions. These elements were designed to help orient and guide the undertaking of framework's second dimension, which is described in further detail as follows.

The second dimension of this study's UProd was comprised of two main elements, which were collectively used to identify how an envisioned SB product might impact the social well-being of Albertans. The **first** element requires the assessor to identify the potential economic and environmental implications surrounding the product of interest and the **second** element requires the assessor to identify the ethical concerns surrounding that same product.

Table 6.19 describes the rationale for having chosen to identify the risks and benefits (implications) surrounding these two elements.

TABLE 6. 19 THREE ELEMENTS COMPRISING THE UPROD FRAMEWORK'S SECOND DIMENSION

Element	Rationale
ACTION 1:	
Identify the potential *economic* and *environmental** implications (risks and benefits) that the emergence of an envisioned SB product of interest might have on the Albertans. These should be considered separately for each stakeholder.	Economic and environmental factors are important determinants of a population's health and social well-being. As such, this action could help provide insight on how an envisioned SB product might impact a population's social well-being (156)
ACTION 2:	
Identify ethical considerations surrounding the emergence of an envisioned SB product of interest on the Albertan population using Mepham's approach to ethical analysis.	Envisioned SB products may challenge common moral principles and their emergence may have moral consequences for society, which justifies the investigation of ethical consideration. Decision-makers are often expected to balance societal interests and ethical analysis can help provide insight into these issues (457)

* Economic and environmental implications have not been weighted. While they are listed together, they were assessed separately in the upstream assessment framework.

Now that the study's upstream product assessment framework has been presented, the findings that resulted from its implementation can now be explored (section 6.4).

6.4 UPSTREAM PRODUCT ASSESSMENT FINDINGS

The present section is divided into two main sub-sections. The first sub-section (6.4.1) describes the findings that emerged from the framework's first dimension and the second sub-section (6.4.2) presents the findings that emerged from the framework's second dimension.

Prior to beginning, this author wishes to make clear three main assumptions made about the organism of interest to this study. **First**, this author assumed that the organism would not be a protocell, but a re-engineered form of a well-known microbial host, such as

E.coli or yeast. **Second,** the microbe would be a fermenter, and thus, would require a source of nutrients (a feedstock) in order to produce bio-butanol. **Third**, this feedstock would be Alberta-grown sources of biomass, specifically, agricultural crops.

6.4.1 Findings of the UProd's First Dimension

The present sub-section will describe the findings related to the three "actions", previously described in Table 6.18.

Action 1: Relevant Existing Regulatory Frameworks

Decision makers often use the 'Familiarity Principle' to help make decisions about the safety of genetically modified organisms. According to this Principle, if re-engineered microbes are created using methods that can be considered 'a simple extension of genetic engineering', they should not pose any greater *bio-safety* risk than their unmodified counterpart (75,90,104). Literature indicated that current SB research in bio-fuel production generally involves the small scale re-design of the genetic circuitry in microbial hosts that are well-understood (104). Based on this information, this author made two additional assumptions about this study's product of interest. **First**, it would not likely pose a greater *bio-safety* risk to society than its unmodified microbial counterpart[26]. **Second**, the existing regulatory framework surrounding industrial biotechnology would be a relevant framework from which to seek guidance for undertaking this study. As such, in the paragraph that follows, this sector will be explored in further detail.

Industrial biotechnology can be defined as the use of living organisms and other biological processes to produce bio-based chemicals, materials, and fuels (458). In the Canadian industrial biotechnology sector, safety assessments are conducted on both the **micro-organisms designed to produce** products of interest as well as **the products** those

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[26] A substantial amount of research has been conducted on the bio-safety risks of genetically modified organisms over the years, and thus, it was not made a focus of the UProd assessment.

organisms produce. Based on this knowledge, this author felt it necessary to assess how **1)** the organism and **2)** the bio-butanol it is set to produce might impact the social well-being of Albertans. In essence, the remainder of the UProd assessment was conducted on **two** products, which are hereafter collectively referred to as 'products of interest'.

Action 2: Pros and Cons of Replacing a Conventionally Used Counterpart

This author identified the *fossil fuel-based exploration and refining of gasoline* as a relevant 'conventionally used counterpart' to the products of interest to this study. Several pros and cons of replacing it with the products of interest to this study have been identified and are summarized in Table 6.20 (following page).

Table 6. 20 Pros and cons of replacing a conventionally used counterpart with a synthetic bio-butanol producing microbe

The 'Pros'
• In order to grow, these feedstocks would necessarily consume CO_2 from the atmosphere. As such, this greenhouse gas would essentially become recycled and 'trapped' within a carbon loop (459) • Greenhouse gases (especially CO_2) from off-shore exploration, drilling, combustion, and refining of fossil fuels like gasoline contribute to global warming (460). Global warming has been linked to a breadth of negative impacts on human health and social well-being, such as increases in infectious diseases and negative impacts on agriculture (461). Bio-butanol could help mitigate the effects of global warming because it would be produced by microbes in factories that feed on renewable *feedstocks*. • Fossil fuels are non-renewable, and thus un-sustainable, which means their supply will begin to decline at some point (peak oil) (286). Bio-butanol is a renewable fuel that can be produced using renewable resources. Theoretically, as long as the microbes, feedstocks, facilities, and staff are available, the supply of bio-butanol will never dwindle • Bio-butanol is more efficient than many other renewable fuels (*e.g.* bio-ethanol). It has a high energy content per weight, which makes it a favourable replacement for gasoline (462) • Unlike gasoline, bio-butanol is bio-degradable (153,295)
The 'Cons'
• While bio-butanol produces fewer greenhouse gas emissions per life cycle than gasoline, it still releases greenhouse gas into the atmosphere when combusted (230,463) • 'The organism' would have to consume a feedstock in order to produce bio-butanol. In Alberta, the most likely type of feedstock would be one or several Alberta-grown agricultural products. There are two concerns within this context. o **First,** these products could include animal and human food crops. According to the 'food vs. fuel' dilemma, diverting food crops for use in the production of bio-fuel could negatively impact the global food supply (463,464). As such, this action could negatively impact the health and social well-being of Albertans and the global population beyond. o **Second**, these feedstocks would have to be grown, harvested, and refined on an industrial level. Indeed, while this action could ignite an economic boost in Alberta's agricultural industry, literature has shown that industrial agriculture is a major contributor to climate change and greenhouse gas emissions (464). • Bio-butanol has an unpleasant smell (462)

Action 3: Relevant Stakeholders Identified

Several different Alberta stakeholders were identified as persons that might be positively or negatively impacted by the products of interest to this study. They ranged from service providers (energy companies), technology providers (researchers) and consumers (the Alberta general public) to feedstock producers (farmers), decision makers, funding agencies, non-governmental organizations and non-human living things (animals). While this author originally intended to consider the impacts of the products on all relevant stakeholders, time did not permit. As such, this study limited its focus on two main groups of stakeholders: the Albertan general public (as bio-fuel consumers) and the province's farmers (as feedstock producers).

6.4.2 FINDINGS OF THE UPROD'S SECOND DIMENSION

The present sub-section will begin by describing what economic and environmental implications (risks and benefits) the products of interest could someday have on the social well-being of **a)** Alberta's general public and **b)** Alberta-based feedstock producers (**Action 1,** Table 6.19). It then proceeds to describe the findings related to **Action 2:** ethical considerations on the two groups of stakeholders described previously (Table 6.19).

Action 1: Economic and Environmental Implications Identified

As shown in Table 6.21 (as follows), this author identified several economic and environmental implications the products of interest could have on the social well-being of Alberta's general public.

TABLE 6. 21 ECONOMIC AND ENVIRONMENTAL IMPLICATIONS THE PRODUCTS OF INTEREST COULD HAVE ON THE SOCIAL WELL-BEING OF ALBERTA'S GENERAL PUBLIC

Implication Considered	Bio-butanol Producing Organism	Bio-butanol Transportation Fuel
	Potential Benefits	
ECONOMIC	Presents an opportunity for *innovation* within the province, which could ultimately benefit well-being of all Albertans (465). In particular, the organism could help diversity the largely fossil- fuel dominated Albertan economy.	With government subsidies, bio-butanol could be sold at cost that is lower or equal to fossil fuels (465)
	Potential Risks	
	If food crops are used as a feedstock for the organism, global food prices could increase. This could negatively impact food security (466)	The production costs of bio-butanol, like other renewable fuels, are expected to be very high, which could be offloaded to consumers if government subsidies are not made available. High costs would likely result in low incentive to use the product (466)
	Potential Benefits	
ENVIRONMENTAL	The organism could help mitigate the harmful effects of global warming by reducing the need for off-shore drilling and refining related to the production of fossil-fuel based energy products. (459).	Could cause a net reduction of CO_2 release, which could mitigate the effects of global warming (467). Further, unlike conventional gasoline, bio-butanol is bio-degradable (153,295)
	Potential Risks	
	The organism would be designed to replicate. History of plant bio-technology shows that genetically engineered plants were able to share genes across species and drastically affect ecosystems through genetic pollution. If inadvertently released from a controlled, industrial, setting, the organism could cause 'genetic pollution' (254).	Although net CO_2 emissions from bio-butanol might be lower than fossil fuels, they are still released. Further, other greenhouse gases such as nitrous oxide (major contributor to acid rain) are also released when bio-butanol is combusted. This might offset some of the advantages gained from reduced CO_2 emissions (467)

In the Table that follows (Table 6.22), various economic and environmental implications that the products of interest could someday have on Alberta-based feedstock producers are described.

TABLE 6. 22 ECONOMIC AND ENVIRONMENTAL IMPLICATIONS THE PRODUCTS COULD HAVE ON THE SOCIAL WELL-BEING OF FEEDSTOCK PRODUCERS

Implication Considered	Bio-butanol Producing Organism	Bio-butanol Transportation Fuel
	Potential Benefits	
ECONOMIC	Farmers who produce feedstocks for the organism could see a boost in employment and income; rural economy could be stimulated (*E.g.* a new domestic market for grains and oilseeds) (459,465)	From this context, a feedstock producer would experience similar issues as Alberta's general public (Table 6.21). They could, however, be more susceptible to price variations due to their inherently elevated consumption of fuel.
	Potential Risks	
	If animal feed crops (grains) begin to be used as feedstocks for these organisms, the market price of animal feed could increase (463)	
	Potential Benefits	
ENVIRONMENTAL	From this perspective, a feedstock producer would produce similar issues as Alberta's general public.	From this context, a feedstock producer would experience similar issues as Alberta's general public (Table 6.21). They could, however, be more susceptible to price variations due to their inherently elevated consumption of fuel.
	Potential Risks	
	From this perspective, a feedstock producer would produce similar issues as Alberta's general public.	

Action 2: Ethical Considerations Identified

As shown in Table 6.23 (follows), this author identified several ethical considerations surrounding the emergence of a re-engineered bio-butanol producing microbe in Alberta.

TABLE 6. 23 ETHICAL CONSIDERATIONS SURROUNDING THE EMERGENCE OF A RE-ENGINEERED BIO-BUTANOL PRODUCING MICROBE IN ALBERTA

Stakeholder Point of View:	Principle of: Well-being	Principle of: Autonomy	Principle of: Justice
Environment	The organism should contribute to a net reduction of environmental impact and should not be produced at the expense of non-human life	Bio-diversity and environmental sustainability should be maintained during its production and use	Interests of the environment and non-human life should be respected during the organism's development and use
General Public	Research on the organism, and its use, should be completed on behalf of the public; innovation should be promoted, which includes the encouragement of information sharing (48)	Democratic decision making and deliberation should be undertaken surrounding the organism's potential impacts on Albertans' social well-being	Possible harms and benefits of the organism should be distributed equitably; no sub-group(s) of Albertans should be affected differently be the organism's emergence
Feedstock Producer	The feedstock producer, and associated labourers, should experience adequate income and working conditions while producing the feedstock	Farmers should be given the choice as to whether they want to produce feedstocks for the organism or not	All farmers producing feedstocks for the organism should be fairly compensated by companies purchasing the feedstock; they should receive the same wage for the same quality/quantity of product

As shown in Table 6.24 (follows), this author also identified several ethical considerations surrounding the emergence of bio-butanol transportation fuel in Alberta.

TABLE 6. 24 ETHICAL CONSIDERATIONS SURROUNDING THE EMERGENCE OF BIO-BUTANOL TRANSPORTATION FUEL IN ALBERTA

Stakeholder Point of View:	Principle of: Well-being	Principle of: Autonomy	Principle of: Justice
Environment	The product should be environmentally sustainable, contribute to a net reduction of greenhouse gas, and not exacerbate climate change	Bio-diversity and environmental sustainability should be maintained during its production and use	Interests of the environment and non-human life should be respected during the product's development and use
General Public	Bio-butanol should be safe for human use, and should not be developed at the expense of peoples' essential rights (access to sufficient food, water, health, work rights and land)	The public should be free to choose whether they wish to use the fuel alternative	Possible harms and benefits of the product should be distributed equitably; no sub-group(s) of Albertans should be affected differently be the fuel's emergence. This includes universal affordability
Feedstock Producer	From this perspective, the ethical considerations surrounding the emergence of bio-butanol transportation fuel would be similar to those surrounding the emergence of a re-engineered bio-butanol producing microbe (See Table 6.23)		

6.5 CHAPTER SUMMARY

In this chapter's first section (6.1), the findings that emerged from the study's scoping review were articulated. In the next section (6.2), the findings related to the process used to choose the exemplar product were presented. Section 6.3 described the upstream product assessment (UProd) framework created by this author, and the next section (6.4) described the findings that emerged from its implementation on the exemplar product. In the chapter that follows (seven), the meaning of these findings in light of previous work completed by other researchers will be discussed.

CHAPTER 7: DISCUSSION

The present chapter discusses the meaning of the findings presented in the previous chapter (six) in light of previous work completed by other researchers. The methodologies used to address the study's research questions were relatively new (scoping review) and novel (the process undertaken to choose an 'exemplar' product and the upstream product assessment framework through which that exemplar product was assessed), thus, this author also devotes some discussion to key insights related to those topics.

The findings are discussed in the order they were presented in chapter six. As such, this chapter begins by discussing the methodology used to undertake the scoping exercise as well as the findings that emerged from its implementation (section 7.1). Next, the 'exemplar' Alberta-relevant SB product chosen for assessment is discussed (section 7.2). In section 7.3, the upstream product assessment framework, and the findings that emerged from its implementation, is discussed. In the final section (7.4), the chapter is concluded.

7.1 THE SCOPING REVIEW

The present section discusses the methodology used to undertake the scoping exercise described in chapter five[27] (sub-section 7.1.1). This section is followed by a discussion of the findings that emerged from its undertaking (sub-section 7.1.2).

7.1.1 SCOPING REVIEW METHODOLOGY

This author generally followed the procedural framework for scoping reviews as outlined by Arksey & O'Malley (133). Due to a lack of methodological detail about how to achieve results, this researcher was required to make decisions about *how* to extract data from the literature reviewed (175,177,468). As described in sub-section 5.2.3, to meet the needs of

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[27] Although a scoping review was also undertaken in chapter four, this chapter's discussion is focused on the review carried out to address research question 1 and 1a (see chapter five).

this study, this author chose to implement a 'summative' approach to qualitative content analysis (266). This approach allowed **a)** the frequencies with which products were identified to be calculated (clerical coding of manifest content) as well as **b)** the nature of discourse surrounding envisioned SB products to be explored (latent coding). Collectively, both manifest and latent coding facilitated the emergence of a greater depth of findings, described in further detail in the discussion that follows.

Manifest coding enabled the calculation of frequencies with which products were discussed across the literature examined. In the end, this process highlighted which products were discussed frequently across SB discourse (*e.g.* renewable energy products), those that were discussed only moderately (*e.g.* environmental products), as well as those that were scarcely discussed (*e.g.* science fiction/fantasy products). Certainly, if this study had limited its analysis to recording, and reporting, the frequencies with which products were discussed, it would have indicated only a small portion about the directions SB, as a discipline, could someday take (469). Although labour intensive, the latent analysis of SB product discourse proved a worthwhile endeavour as it allowed this researcher to gain insight into how the discipline's products were 'framed' or presented across the literature examined. This process also resulted in the identification of six emergent themes concerning the nature of SB product visions in general.

The concept of 'framing' will be further explored in sub-section 7.1.2, when the findings that emerged from the scoping review are discussed. The present sub-section continues by discussing the advantages and disadvantages of analyzing the content of documents. It then moves on to discuss on the methodology used to select the documents reviewed in this study.

Analyzing the Content of Documents

As noted by Buttolph Johnson & Reynolds (135), there are several advantages to analyzing the content of documents as a tool through which to study a topic of interest. First, it is an indirect, and thus, non-intrusive form of research. Indeed, while the researcher's perspective *could* influence his or her interpretation of the message contained in a document of interest, their perspective does not bias or influence what is *written* in that document. This author of this study addressed this issue by declaring personal opinions, beliefs, and values that might have impacted the interpretation of the message contained in the documents analyzed. Further, a second reviewer examined the study's findings, and did not note the presence of researcher bias. As such, this author is confident that the findings that emerged from the documents analyzed in this study were truly reflective of the content contained within them.

Another advantage of analyzing the content of documents is that many are relatively easy to access. As such, they are relatively convenient tools on which to conduct research. Certainly, they are also useful for longitudinal studies; they allow researchers to study how topics/situations have evolved over time (135). This study took advantage of this benefit by analyzing the content of documents published on SB between the years 2000 and 2010, inclusive. As such, these findings of this study were robust to the inclusion of a decade's worth of data.

Along with the advantages described previously, in this study, document analysis also carried certain disadvantages. For example, some documents initially retrieved from electronic database searches were automatically deemed ineligible for review because they were not available in full text. This could have biased the sample, and thus, might have limited this study's findings. Having acknowledged this issue, this author examined and compared the descriptive characteristics of those documents (n=37). In the end, this researcher found those documents varied in type, country of origin, and year published. As such, while at least a portion of those documents might have been includable, their unavailability did not likely bias the sample of documents ultimately chosen for review.

Type of Documents Sought

Many researchers consider scientific publications, especially peer-reviewed journal articles, the best means through which to understand matters of science (470). In order to gain a more comprehensive understanding of science and technology (*e.g.* how an emerging technology might be perceived by society), Schmidt *et.al.* (234) have noted that a variety of world-views should be consulted. This notion was the impetus for the decision to analyze the content of three types of documents: **scientific** (peer-reviewed journal articles), **governance/ policy** (reports), and **media** (newspaper and magazine articles) in this study.

While journal articles and governance reports tend to be written for a specific type of audience (*e.g.* researchers and decision makers), the audiences reached by the media can be quite diverse (471). Indeed, the media is usually the most available, and sometimes only, source of information about scientific discoveries and controversies for many members of the public (472). In the end, communication mediators**,** such as journalists, educators, and opinion-makers help filter and shape the information presented (473). As such, not only is it informative to study *what* is being said about a topic of interest, but also the *way* in which it is discussed.

Numerous world-views and perspectives about SB's envisioned products were represented across the three types of documents analyzed in this study. As such, a more robust understanding of SB's product visions was gained than might have been possible if the content of only one or two types of documents was scoped. Further, by identifying **a)** what envisioned SB products were discussed **and b)** the nature of discussion surrounding them, this author was able to gain a deeper understanding of *how* the discipline's products were portrayed (see sub-section 7.1.2). In policy-relevant studies such as this, previous researchers have noted that these two steps can help highlight what information is presented to decision makers. As such, this study has gained insight into what factors might have already influenced decision making within the context of SB's product visions (474,475).

Document Searches

As described in section 2.2, in addition to 'synthetic biology', the term 'synthetic genomics' is regularly used across the scientific community to describe the branch of biotechnology studied in this thesis. Although none have become widely adopted, the discipline has also acquired a variety of synonyms over the years, largely in an attempt to avoid the term 'synthetic' (57). While this author was aware of several synonyms and other descriptive terms used to describe SB, in this study, only documents that contained the terms 'synthetic biology' or 'synthetic genomics' were eligible for review.

A large number of documents (N=2847) were initially retrieved from electronic databases by searching for literature on SB using the two keywords described above. Despite this, it is possible that some product visions might have been overlooked or underreported and some emergent themes might have been missed because keyword searches were limited to only two terms. Indeed, a broader perspective on the discipline's product visions might have been gained by expanding searches to include synonyms and other relevant keyword combinations such as "constructive biology", "artificial life" and "designer AND organism" (476).

A recent content analysis study of SB coverage in German-language media (476) revealed the utility of expanding keyword searches to include a variety of other relevant terms. In their study, Gschmeidler & Seiringer (476) noted that many German media articles (35% of their sample) published since 2004 dealt with SB, but did not mention the term directly. While the language of report might have played a role in their findings, this author suggests that future English-language studies on the discipline broaden keyword searches to include a wider range of relevant terms.

7.1.2 Scoping Review Findings

This sub-section is divided into three main parts. The first will discuss the included documents' descriptive characteristics. Next, the envisioned products identified during the clerical coding process will be discussed. The final section is devoted to discussion surrounding the study's emergent themes.

Included Documents' Descriptive Characteristics

All of the documents sought for this study's scoping exercise were required to have been published a) in the English language and b) between the years 2000 and 2010, inclusive. Of the documents initially retrieved from searches (N=2847), the annual number generally increased each consecutive year. At least two other studies that examined news media coverage of SB over time (105,476) have noted similar overall trends. Given these findings, this author expected that the final number of articles included for review (n=367) would follow the same trend, which proved to be generally true. As shown in Figure 6.4, number of articles scoped in this study increased across each publication year from 2004 to 2010 (inclusive), with the exception of 2008.

While this author did not expect the number of included articles published in 2008 to be lower than those published in the previous year (n=59 in 2007 compared to n=53 in 2008), the difference was very small (six articles). As such, this author was not overly concerned about the potential for selection bias. Indeed, the drop in articles analyzed from 2008 could have simply been due to chance, as a random number of eligible magazine and peer reviewed journal articles were selected for review (see sub-section 5.2.2).

As further illustrated in Figure 6.4., of the n=367 articles actually scoped in this study, none were published between the years 2000 and 2003, inclusive. This author was not surprised by this finding. Although many cite the year 2000 as the time that SB officially emerged as a discipline, research in the field was only pursued aggressively since 2004 (237).

Given the United States' current dominance in SB (43,104-107) this author was not surprised that the largest proportion of articles reviewed in this study (47%) originated from that geographical area (Figure 6.3). This author contributes these findings to the fact that the country took an early geographical lead in SB research (see section 2.5). To date, United States-based researchers remain the most dominant players in the field based on number of scientific publication and amount of public and private funding sources (104,107).

Figure 6.2 illustrates the percentage of identified articles deemed relevant for review because they mentioned or discussed at least one envisioned SB product. Generally, this study found that the number of journal articles deemed relevant for review on this basis increased annually; however, only a small proportion of journal articles initially retrieved were actually eligible for review on this basis (an annual average of 36%). These findings could be due to an increase in the annual amount of *results* produced by SB researchers around the world. More results translate to a greater knowledge-base, which could also mean field's practitioners are closer than ever to being able to create the synthetic products they envision. Especially when applying and competing for research grants, synthetic biologists might also be feeling pressure to emphasize or 'hype' the field's product promises.

In contrast to journal articles, a greater proportion of media (magazine and newspaper) articles initially retrieved for review mentioned or discussed envisioned SB products over time. On average, more newspaper articles mentioned or discussed at least one SB product vision than magazine articles (an annual average of 85% compared to 71% of articles, respectively). A recent study by Kronberger *et al.* (477) provides some insight into these findings. According to that researcher, many journalists believe SB is only newsworthy if specific applications can be discussed. Indeed, envisioned SB products appear to 'matter' to the public (their audience), and the discipline is becoming increasingly understood in terms of those product visions (477). In order to attract and retain readership, this study's findings have shown that journalists writing on SB appear to have become cognisant of this need.

Envisioned Products Identified

Table 6.1 provided a numerical breakdown of the frequency with which envisioned SB products were discussed across the documents analyzed in the scoping study. The most frequently discussed type of envisioned products were related to the production of renewable energy (78% of articles reviewed) and one of the least discussed types of products related to defence applications (7% of articles). Envisioned human health products were identified as the second most frequently discussed type of SB product (67% of articles), followed by industrial and environmental applications (42 and 30% of articles, respectively). This author was able to gain some insight about the meaning of these findings by drawing upon the work of two previously published studies (105,476). While useful, the insight gained from these studies was limited because their analysis was restricted to SB coverage across American and European newspapers. Nonetheless, the discussion that follows will explore these findings in further detail.

A 2008 study by Pauwels & Ifrim (105) revealed marked differences in the frequency with which envisioned SB products were discussed across European and American newspapers. While energy-related SB products were given a similar amount of attention in both American and European newspapers, in European newspapers, the authors found that envisioned environmental applications were discussed more frequently than human health products. By contrast, human health applications were mentioned more frequently in the American press than envisioned environmental applications (105). These authors asserted the differences in coverage might be reflective of the priority differences across the two locations.

In terms of overall biotechnological focus and priority, the United States is predominantly oriented toward the health care sector and evidence suggests that American citizens consistently view health care to be more important than matters of the environment (478,479). By contrast, European debates concerning the environment generally follow a precautionary stance, and polls have shown that European citizens tend to view climate change as a more significant global problem than the spread of disease (153,357,480). Certainly, these priority differences might have caused the news media to discuss envisioned products of 'greatest priority' to their geographical audience (105).

Pauwels & Ifrim's (105) findings offer some insight into the findings that emerged from this study's scoping exercise. As shown in Figure 6.3, nearly half (47%) of the articles analyzed in this study originated from the United States. Further information taken from that Figure 6.3 and Table B.1 indicates that n=118 or 32% of the articles analyzed in this study originated from Europe. Based on geographical origin alone, the findings of Pauwels & Ifrim (105) suggest that, in this study, human health applications should have been discussed more frequently than environmental applications. Indeed, this study's findings concur with this postulation.

In their recently published study on German-language newspaper coverage of SB, Gschmeidler & Seiringer (476) noted that no envisioned agricultural applications were mentioned in the articles they analyzed (476). By contrast, in this study, 10% of the articles analyzed mentioned or discussed at least one envisioned agricultural application of SB. A few factors could account for this difference. First, this study analyzed articles that originated from numerous different countries (Table B.1, Figure 6.3) whereas Gschmeidler & Seiringer (476) limited their analysis to German-language articles. Given the wide range of governmental, economic, and social priorities throughout the world, it is likely that some applications would be of greater priority to some geographical areas than others (136). In Canada, agricultural biotechnology has historically been a greater priority than other areas, such as health biotechnology (479). Given that 18% of articles (n=66) analyzed in this study originated from that country, this author is not surprised by the number of envisioned environmental applications identified. Indeed, it could be that the agricultural sector is simply not as great a priority for countries where German is spoken.

Emergent Themes

Human perceptions, especially hope, are fundamental to the acceptance and advancement of novel technologies (481). As noted by Aldrich *et.al.* (395), if experts in an emerging field can demonstrate that their technology shows promise to achieve wide societal benefit, advancement is rarely refused. This apparent need to gain "public buy-in" (481) was not only reflected by the frequency and range of products identified during this analysis, but by the apparent de-emphasis, and even downplay, of the risks associated with them. As noted by Newman *et.al.* (303), "technologies of dubious value won't move people to understand and embrace them".

At SB's early stage of development, the way in which the discipline is portrayed in literature can offer insight into how both proponents and opponents of SB 'frame' their issues (105). In this study, the literature generally appeared to hype the discipline; an array of product promises was identified and many documents attempted to instil a deep sense of social hope in the discipline (28,295,303,396, 481,482). Similar findings have also been noted in the work of others (332). de Vriend (104) postulated that journalists might be prone to over-estimate and over-emphasize the potential benefits that SB could bring society. Further, as noted by Lopez (483), hype is relatively common in science and technology discourse; this type of inflated 'storytelling' can also be designed to help researchers gain monetary support for their work (119,426,483).

Previous work by Nisbet *et. al.* (484) has noted that public attitudes about science are largely driven by the way information is 'framed'. For example, a member of the lay public would likely respond differently to a newspaper article on SB based on the way a journalist chose to 'frame' or emphasize the information presented about it. Certainly, if journalists generally choose to emphasize SB's potential to create numerous beneficial products for society, readers would likely accept the research. Conversely, if journalists choose to emphasize SB's risks, and portray synthetic biologists as arrogant Dr. Frankensteins, society might be more inclined to reject the discipline.

Previous research has shown that biotechnology coverage in the media tends to favour the interests of scientists, industry, and government, which are generally "pro-technology and pro-research" (484). These findings generally concur with those of this study. Indeed, while this author identified several articles that mentioned or discussed at least one risk related to envisioned SB products, in general, the discourse emphasized their potential benefits.

From religious references such as 'playing God' to notions of SB practitioners creating 'Frankenstein' bugs, this study noted the emergence of several literary devices (particularly metaphors and similes) during data analysis. Previous work offered insight into the meaning of these findings. Nelkin (485) noted that, when information about unfamiliar technical material is provided to members of the non-expert public, metaphors can often be used to help reach audiences using familiar constructs. In essence, metaphors act as literary tools, providing a "richness of reference" (485) for the reader. Indeed, metaphors can help connect complex science and technical information with readers in more culturally relevant ways (485,486).

In his 2009 study, van den Belt (433) noted that journalists often use the metaphor "playing God" when they report on new developments in the life sciences. This, that author asserted, is often "closely entwined" with the theme of 'Frankenstein', which generally agrees with the findings of this study. While the religious metaphors identified during the scoping exercise generally related to ethical questions about whether scientists should attempt to create (or tinker with) living organisms, the term Frankenstein was generally used to emphasize the potential 'monstrous' outcome of those undertakings (476).

Several other studies have noted the occurrence of these literary devices within the context of SB as well (56,206,426,433,476). In their 2009 study, Cserer & Seiringer (206) noted the rhetorical use of metaphors such as 'playing God' and the use of the term Frankenstein in nearly every German-language newspaper article they analyzed. In a more recent German newspaper study, Gschmeidler & Seiringer (476) also noted that SB discourse was "rich in stylistic devices" such as those described above.

7.2 Exemplar Alberta-Relevant Synthetic Biology Product

As described in Table 3.1 and section 4.3.2, this author developed and implemented an evidence-based process through which this study's exemplar 'Alberta-relevant' SB product was chosen. Despite these efforts, this author acknowledges that it is inherently difficult to predict the fate of emerging technologies. Indeed, this product currently remains in the research and development phase and it may never become realized.

One of the factors taken into consideration during the 'product identification' process was current and historical Alberta-based SB research (Table 6.17). This author made the assumption that, since SB research on bio-butanol had a history in Alberta, that product might be more likely to impact the province's citizens over products without a research history in the province. In reality, numerous SB products could someday impact the lives of Albertans. Indeed, those products might even be *more likely* to impact the lives of Albertans.

As noted in a 2011 policy brief by the Rathenau Instituut (487), the first commercial application of SB could be the production of vaccines. If this turns out to be the case, millions of Albertans could be impacted by this product within the next few years. Further, oil companies are to re-claim the sites they explore, which usually entails digging up contaminated soil and trucking it to landfills. Certainly, while these actions might fulfill their 'clean-up' requirements, it simply moves the contamination from one point to another. SB could be used to address this problem through the creation of custom-made bio-remediation devices, designed to metabolize contaminants from the soil and create a harmless bi-product in return.

If this type of SB product were successful, Alberta could become a world leader in SB-based bio-remediation technologies.

7.3 Upstream Product Assessment Framework (UProd)

This section is divided into two main parts. The first sub-section (7.3.1) discusses the framework itself, and the next sub-section (7.3.2) discusses the findings that emerged from its implementation.

7.3.1 The UProd: Design and function

This study's UProd was designed to help pinpoint relevant information about how an Alberta-relevant SB product might someday impact the social well-being of Albertans. In the end, this framework was successful in facilitating information-gathering; a preliminary, but essential, first step in the decision-making process. Indeed, it was not created to help predict the future, and its findings should not be considered fact. While a decision making tool, UProd was **not** designed to be a 'decision maker'. If its findings are continuously supplemented, the UProd could be used to help *design* the future of SB-based bio-butanol production in Alberta.

This author acknowledges the inherent difficulties associated with proactive or upstream exercises. Because the exemplar product assessed in this study does not yet exist, this author was left wondering whether some of the issues identified during UProd's implementation could be trusted or whether they were even relevant. As noted by Tucker & Zilinskas (43), some of SB's risks are "simply indefinable at present". Indeed, SB's envisioned products might also carry implications that no one can anticipate with any degree of certainty at the present time- even if the right questions are asked.

The framework's second dimension (see Table 6.19) was designed to facilitate the identification of relevant information that could be used to address each of the 'cells' contained in Tables 6.20-6.23. Although a wide range of relevant information was retrieved from documents identified during that 'data gathering' process (see Table 5.1), this author acknowledges the limitations associated with this methodology. For example, some key documents might not have been available for analysis, or might not have been identified during the data gathering process, which could have limited the study's findings. Further, society (and thus, the Alberta population) is composed of several subgroups of people with various cultural, religious, and fundamental values (233). By limiting information sources to published documents, this study might have overlooked some important considerations within these contexts.

To help gain a wider perspective of views and opinions on the matters addressed in this study's UProd, this author suggests that a second step be undertaken to supplement its findings: a participatory exercise using focus group discussion. As noted by Kuzma & Tanji (54), "safe, adequate, just, and appropriate policies for [SB product] oversight can only be designed through wide-scale deliberation" (54).

7.3.2 UPROD FINDINGS

At first glance of the findings that emerged from the UProd assessment, the exemplar product might be interpreted as a winning solution to society's current challenges. Indeed, the product has an enormous potential to provide 'clean' alternative energy for Albertans. As such, it could help address the environmental concerns associated with Alberta-based oil and gas exploration and could help diversify the largely fossil-fuel dominated Albertan economy. It also presents an opportunity for innovation within the province and could strengthen its agricultural sector. Upon closer examination of the findings, however, this author took a more critical perspective of the product and questioned its actual potential to provide a net positive benefit for the social well-being of Albertans.

The product assessed in this study does not address one of the fundamental problems associated with the current energy crisis: over-consumption. Rather than creating a product to replace dwindling fossil-fuel-based energy products, this author believes Albertans' social well-being would benefit more from a) more extensive use of public transportation, b) better driving habits, and c) improvements in vehicle efficiency. In the end, these might even prove to be less costly and efficient ways of addressing climate change.

This author is also concerned about the organism's design to ferment Alberta-grown agricultural crops, such as grain. According to the Alberta government, Albertans currently only consume ~1% of grains and oilseeds that could be used in the manufacturing of renewable fuel (488). As such, from the government's point of view, the price of food would not likely be impacted by using Alberta-grown grain as a feedstock to produce bio-fuel (488). According to the 'food vs. fuel' dilemma, however, diverting food crops for use in the production of bio-fuel could negatively impact the *global* food supply (463,464). As such, even if this action does not directly impact the social well-being of Albertans, it *could* impact the well-being of global populations. The United Nations holds a particularly strong viewpoint on this topic, maintaining that it is "a crime against humanity to convert agricultural productive soil into soil which produces food stuff that will be burned into biofuel" (489).

This author is also concerned about the organism's design to ferment Alberta-grown agricultural crops because they would have to be grown, harvested, and refined at an industrial level. While this action could ignite an economic boost in Alberta's agricultural industry, literature has shown that industrial agriculture is a major contributor to climate change and greenhouse gas emissions (464). In the end, the production and use of 'clean' bio-butanol might be just as harmful to the health and social well-being of Albertans as burning fossil fuels.

7.4 Chapter Summary

This chapter discussed the meaning of the material and findings presented in the previous chapter (six) in light of previous work completed by other researchers. This chapter began by discussing the methodology used to undertake the scoping exercise as well as the findings that emerged from its implementation (section 7.1). Next, the 'exemplar' Alberta-relevant SB product chosen for assessment was discussed (section 7.2). In section 7.3, the study's UProd, and the findings that emerged from its implementation, was discussed. In the chapter that follows (eight), the study is concluded.

CHAPTER 8. CONCLUSIONS, FUTURE WORK, AND CONTRIBUTIONS TO KNOWLEDGE

The present chapter concludes the study. It begins by reviewing the study's objectives (section 8.1) and proceeds to describe how the work presented in this thesis met those objectives (section 8.2). Next, section 8.3 provides study conclusions, section 8.4 provides suggestions for future work, and the final section (8.5) summarizes the study's contributions to knowledge in the fields of SB, upstream technology assessment, and scoping review methodology.

8.1 REVIEW OF THESIS OBJECTIVES

Defined by this study's research questions, the general objective this thesis was to better understand how envisioned SB products might someday impact the lives of Albertans. To meet this objective, this thesis addressed four separate goals:

- To **identify** what SB product predictions were made since the field's emergence in 2000, including the nature of that discourse;
- To **develop** a set of criteria that could be used to 'filter' out an 'exemplar' product of relevance of Alberta;
- To **develop** an upstream assessment framework through which the potential impacts of that exemplar product could be identified; and
- To **implement** that upstream assessment framework on the exemplar product of interest to identify the implications the product might someday have on the social well-being of Albertans.

8.2 MEETING OBJECTIVES: THE CONTRIBUTIONS OF THE THESIS

Chapter three delineated the basis of thought and courses of action required to address the study's central research question. It played a key role in structuring the study's overall design, and thus, the execution of the literature scoping exercise undertaken in the chapter that followed (four).

In chapter four, knowledge gaps related to two topics areas of particular relevance to the study were identified, specifically: 1) scoping or surveying SB's product visions, and 2) assessing the potential impacts that an envisioned SB product might have on a population of interest. Briefly, this author found that no previously published studies had attempted to transparently and systematically identify envisioned SB product visions over time. Further, while one study (198) was found to have performed a proactive product assessment that aligned somewhat with the aims of this study, its lack of methodological detail about how to achieve results created a knowledge gap that required further exploration on the part of this researcher. Toward this end, two additional research questions were developed to address these research gaps:

1) What SB products have been envisioned since the year 2000?
    1a) What is the nature of that discourse?
2) Of SB's envisioned products, which might be of particular relevance to the Province of Alberta?
    2a) How might an 'exemplar' product of relevance to Alberta impact the social well-being of its citizens?

This chapter also identified the criteria used to develop the study's upstream product assessment framework (UProd).

The methods used to address the study's research questions were discussed in chapter five. Briefly, this chapter outlined the research parameters required to **a**) undertake a scoping review of the literature to identify envisioned SB products, **b)** identify an Alberta-relevant envisioned SB product, **c)** to develop the upstream product assessment framework, and **d)** to implement that framework.

In chapter six, the study's findings were addressed. Briefly, a scoping review identified N=117 distinct envisioned SB products across eight main application areas in addition to six main emerging themes related to those products. Further, in this chapter, an Alberta-relevant emerging SB product was identified, and was subsequently used as the 'exemplar' product upon which the UProd framework was implemented. It was identified by carefully considering: **a)** existing SB research in Alberta, **b)** the province's political and economic landscape, **c)** Alberta's research and innovation priorities and **d)** Albertan public opinion. The upstream product assessment of bio-butanol (using 'synthetically' re-designed microbes) was examined from the perspective of many stakeholders. In the end, this assessment resulted in a clearly disseminated overview of the risks and potential benefits that bio-butanol, and the synthetically re-engineered microbes that might someday produce it, could someday have on Albertans' social well-being.

8.3 Study Conclusions

The scope of SB's product visions is broad and its proponents are very hopeful about the benefits they could someday bring society. In the short term, SB practitioners are expected to re-design a variety of well understood organisms proficient in producing industrial chemicals. Longer-term product predictions entail the complete synthesis of novel living systems that do not exist naturally. Indeed, these complex synthetic 'machines' could be designed to perform a variety of specialized tasks from scavenging and destroying tumours, enhancing the nutritional properties of crops, and cleaning up our environment by digesting toxic waste.

Many envisioned SB products could someday impact the lives of Albertans; however, re-engineered bio-butanol producing microbes are, perhaps, one of the most relevant SB products to that province and its citizens. According to this study's UProd, if this technology became a reality in the Province of Alberta, it could impact the social well-being of the province's citizens both positively and negatively.

For example, if Alberta-grown agricultural products were used as feedstock for these microbes, it could ignite an economic boost in Alberta's agricultural industry. On the other hand, diverting agricultural crops for this use could negatively impact the global food supply. Further, the industrial processes needed to grow, harvest, and refine those crops could contribute substantially to climate change. Certainly, at least some of the harmful effects of global warming would be reduced if gasoline were replaced with bio-butanol because the need for off-shore drilling and refining (of fossil fuels) would be reduced.

Fundamentally, re-designed bio-butanol producing microbes do not address one of the fundamental problems associated with the current energy crisis: over-consumption. In the end, the synthetic production, and use, of 'clean' bio-butanol might be just as harmful to the health and social well-being of Albertans as burning fossil fuels.

8.4 Suggestions for Future Work

This author identified six main limitations of this study, each of which can be addressed with future research. First, more than half of the articles reviewed during the scoping exercise were media-based (*e.g.* from magazines and newspapers). As a result, the study's findings could be inherently biased or contain incomplete information. Future studies could address this limitation by scoping a greater number of non media-based documents.

The second limitation of this pertained to the literature search delimitations: English-language documents published between the years 2000 and 2010. Limiting the articles examined in this study to those published in the English-language introduced the potential for language bias. This was of particular concern given that at least three potentially relevant articles were excluded on the basis of language (490-492). Further, the discipline is gaining increased popularity in countries where English is not the dominant language. The large number of English-language articles written on the discipline, however, indicated that a very active, and arguably most predominant, discussion on SB research exists in the English language.

In addition to language considerations, the wide date-range of articles (2000-2010, inclusive) scoped to address this study's research question was also of concern. Given that SB is an emerging technology, the information retrieved from this review could potentially become out of date as quickly as the work was completed. This author encourages future studies to address this study's literature search delimitations by 1) scoping a wider range of foreign-language literature for envisioned SB products, and 2) continuing to scope the literature for envisioned products over time to ensure the information is kept up to date.

This author noted a third limitation of this study that pertained to the *quality* of information retrieved from the articles scoped. While the scoping study identified a vast quantity of envisioned products discussed in the literature, it did not attempt to measure the *quality* of those product visions. For example, this study did not attempt to determine the level of evidence at which SB's product predictions were made. As suggested by Grant & Booth (176), a lack of quality assessment in scoping reviews could limit decision makers' uptake of the findings.

While this study did not address the quality of each product prediction, it did not overlook this matter altogether. As noted in chapter six, this research did differentiate between product visions considered 'science fiction or fantasy' from those this author considered at least possible. The Ratheneau Institute's de Vriend (104) pointed out the importance of carrying out such a process as a first step in decision making because it could help focus policy discussion around those that are more likely to impact society. Nonetheless, this researcher suggests that future steps should be taken to assess the quality of product predictions made over time.

The fourth limitation of the study identified by this author was the inherent uncertainty associated with SB's envisioned products. Indeed, it is certainly impossible to identify *all* of the risks and benefits associated with a SB product before it is developed (426). While it may be impossible to predict all of the possible implications envisioned SB products might someday bring to society, these efforts must not be dismissed as a waste of time. Indeed, oversight of this nature might someday save lives and it could help shape the future of SB products in society. As such, this author encourages future work within this area to continue.

A final study deficit identified by this author pertained to the study's UProd. While undertaking the assessment, a lack of knowledge existed on the values, beliefs and interests of Albertan stakeholders. Its findings would benefit from accessing information sources other than published documents. This author suggests the use of focus groups. Indeed, this could both improve information input and would confer more legitimacy on the process.

On a final note: the focus of this study's upstream product assessment was bio-butanol produced by re-engineered microbes. In order to test the wider applicability of the framework, it should be tested on other envisioned SB products. Further, the framework should be updated on an ongoing basis. Indeed, as noted by a 2010 International Risk Governance Council report, "any effective approach to risk governance of SB must be capable of evolving as scientific and technical knowledge expands" (151).

8.5 SUMMARY OF CONTRIBUTIONS TO KNOWLEDGE

This research contributes knowledge on SB product visions and provides further insight on undertaking scoping reviews and proactive technology assessments. Specifically, the results of this thesis can help make those interested in, but not intimately familiar with, SB aware of the products the discipline's practitioners envision for the future. Further, this study illustrates how qualitative content analysis can be used to meaningfully chart and summarize data and concepts in a scoping study. Additionally, this research provides insight on conducting upstream technology assessments by illustrating the successful development and application of such an assessment and tool.

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APPENDIX A: INFORMATION SUPPLEMENTARY TO STUDY METHODOLOGY

A.1 INVENTORY OF ORGANIZATIONS KNOWN TO PUBLISH ON SYNTHETIC BIOLOGY

TABLE A. 1 LIST OF ORGANIZATIONS KNOWN TO PUBLISH ON SYNTHETIC BIOLOGY*

Country	Organization Name (Location of Headquarters)
Canada	ETC Group (Ottawa)
United States	**Bio Economic Research Associates (Massachusetts, Vermont);** Central Intelligence Agency (Virginia); **Edge Foundation, Inc. (Unknown, American founder);** Friends of the Earth (Washington, D.C., California); **J. Craig Venter Institute (Maryland, California)**; National Academy of Sciences (Washington, D.C.); **National Institutes of Health (Maryland);** National Science Advisory Board for Biosecurity (Maryland); **Office of Science and Technology Policy (Washington, D.C);** The Presidential Commission for the Study of Bioethical Issues (Washington, D.C.); **Goldman School of Public Policy (University of California, Berkeley);** SynBERC (Synthetic Biology Engineering Research Council) (California); **The Hastings Centre (New York);** The National Academies (KECK Futures Initiative) (California); **U.S. Department of Energy (Washington, D.C.);** Woodrow Wilson International Centre for Scholars Synthetic Biology Project (Washington, D.C.)
Europe	**Biotechnology and Biological Science Research Council (BBSRC) (United Kingdom);** Centre for Synthetic Biology and Innovation (Imperial College, London) (United Kingdom); **Church of Scotland Church and Society Council (United Kingdom);** European Commission (Belgium); **Federal Ethics Committee on Non Human Biotechnology (Switzerland);** Health and Safety Executive (HSE) (United Kingdom); **International Association Synthetic Biology (IASB) (Germany);** International Risk Governance Council (Switzerland); **Institute for Science and Society (University of Nottingham, United Kingdom);** Lloyd's (United Kingdom); **NEST- New and Emerging Science and Technology (Belgium);** Parliamentary Office of Science and Technology (United Kingdom); **Rathenau Institute (The Netherlands);** Royal Academy of Engineering (United Kingdom); **Swiss Federal Institute of Technology Zurich (ETH Zurich) (Switzerland);** The Foundation for Science and Technology (United Kingdom); The Royal Society (United States); **The Royal Society of Chemistry (United Kingdom);** Towards a European Strategy in Synthetic Biology (TESSY) (Belgium); **Wellcome Trust (United Kingdom);** World Health Organization (Switzerland); **Organization for International Dialogue and Conflict Management (Austria)**

* This list is not exhaustive

A.2 Breakdown of Excluded and Included Articles

Table A.2 provides a numerical breakdown of articles excluded by type. It also highlights the number of articles initially deemed eligible for review as well as the *actual* number of articles reviewed.

Table A. 2 Numerical breakdown of articles excluded and included from review, by type

	Newspaper Articles	Magazine Articles	Journal Article	Reports	Total
Original # Articles Retrieved	**n=265**	**n=399**	**n=2116**	**n=67**	**n=2847**
Exclusion Criterion: Lack of Access to Information					
Full text not available at time of Review	n=1	n=19	n=17	-	**n=37**
Text not readable in ATLAS.ti	-	n=7	n=4	-	**n=11**
Exclusion Criterion: Duplicates, Language, and 'Other' Exclusions*					
Duplicate Articles	n=65	n=17	n=1164	-	**n=1246**
Article not in English	-	-	n=17	-	**n=17**
Other Exclusions*	A (n=4)	B (n=2)	C (n=38)	D (n=41)	**n=85**
Exclusion Criterion: SB, SG, and Envisioned Products and Applications					
SB or SG did not appear in main text	-	n=21	n=254	-	**n=275**
No products or application areas discussed	n=40	n=93	n=347	-	**n=480**
Total # articles excluded	**n=109**	**n=159**	**n=1841**	**n=41**	**n=2150**
Articles Eligible for Review					
Total # articles eligible	**n=155**	**n=240**	**n=275**	**n=26**	**n=696**
Total # articles reviewed	**n=155**	**n=90**	**n=96**	**n=26**	**n=367** (13% of original)

* Other exclusions: **A**: Magazine article (**n=1**); news summary (**n=2**), **B**: Book review (**n=1**); newsletter (**n=1**), **C**: Conference/meeting paper (**n=22**); journal preview/editorial (**n=16**); **D**: SB not discussed in significance (**n=27**); no discussion of SB governance/policy (**n=14**)

A.3 THESIS CODEBOOKS

This author created two codebooks that were used to guide the systematic extraction of data from the articles analyzed. The first (Table A.3) was used to facilitate the extraction of simple publication details whereas the second codebook (Table A.4) was used to facilitate the extraction the study's manifest and latent content.

TABLE A. 3 THESIS CODEBOOK: SIMPLE PUBLICATION DETAILS

Code Type	Explanation
CODE 1: Document Identification *Record in Excel Logbook Column A*	Type the identification number of the article being examined: • Magazine articles begin with **M1**, and are numbered consecutively as follows: **M2**, **M3**, **M4**, *etc*... • Newspaper articles begin with **N1**, Journal articles begin with **J1**, and reports begin with **R1**
CODE 2: Document Classification *Type in Excel Logbook Column B*	Record the **type** of article examined. • Examples include: (Newspaper articles: News, Comment, Feature; Magazine articles: feature, news; Journal article: research note, letter, review article; Report: policy brief, concept note) **Do not guess**. If the article type is not explicitly stated do not record one.
CODE 3: Authors, Author Affiliation, and Date Published *Type in Excel Logbook Columns C, D, E*	**Column C**: record the author(s) using the following structure: Last Name, Initials. **Column D**: Journal articles: record author's or authors' geographical affiliation(s). For newspaper articles, record the geographical location of the newspaper headquarters; Reports: record the geographical location of the headquarters. Magazine articles: record the geographical location of the newspaper headquarters. **Column E**: record the article's publication date as follows: December 15, 2010.
CODE 4: Document Title (in FULL) *Type in Excel Logbook Column F*	Type the document title **exactly** as found on document • Preferably, **copy and paste** it from the source document.
CODE 5: Publication Source (Name) *Record in Excel Logbook Column G*	Record the **EXACT** title of the publication. Examples include: • Scientific American **or** Time; Nature Biotechnology; The Guardian or The Telegraph Journal; International Risk Governance Council

Table A.4, below, is the codebook that was used to facilitate the extraction the study's manifest and latent content.

TABLE A. 4 THESIS CODEBOOK: MANIFEST AND LATENT CONTENT

Code Type	Explanation
CODE 6: Identify future SB products and/or application areas <u>(Manifest Content)</u> *Code using ATLAS.ti**	Use qualitative content analysis methodology to perform the following tasks. • Scan the article's full text to determine whether it 1) mentions or 2) discusses a **specific SB product,** such as "cellular pharmaceutical factories", or SB "cancer scavenging machines", select the name of **each product** discussed and **code each one <u>separately</u>** as an 'in-vivo code'. The text itself will become the name for the code, so **DO NOT** code too many words, just the name of the product. • If the article discusses a **specific application sector** in which SB products could someday be applied (*e.g.* agricultural applications, environmental applications), select **each application sector** and **code each one <u>separately</u>** as an 'in-vivo code'. Again, the text itself will become the name for the code, so do not code too many words, just the application sector(s) mentioned
Identify the *nature* of discourse surrounding the specific SB products and application areas: <u>(Latent Content)</u> *Code using ATLAS.ti**	As you read article discussion around **specific possible SB product(s)** or **application sector(s)**, you might notice the emergence of certain themes. • *E.g.* as you read articles, you might notice time and time again that the same **SB companies** are mentioned. OR, you might notice that **the same people discussed** within these discussions. **STEP 1:** • As themes are discovered, identify the textual exemplar (text that illustrates a theme) **STEP 2:** • Highlight the exemplar and assign either a novel, or already used, theme code. o **NOTE**: Codes should be concise but not too cryptic. ***E.g.*** it is better to assign a code like **Theme-Economics** than theme Pertaining to Economics **NOTE**: consult the '**Coding by list**' option in Atlas.ti before creating a new code name to ensure that **'double dipping'** does not occur.

* If ATLAS.ti is not available, copy and paste the text you would have highlighted and assigned a code to and place it in a clearly marked Word document

Appendix B: Information Supplementary to Findings

B.1 'Other' Countries of Origin Represented in Articles Included for Review

In addition to reviewed articles that originated from the United States (47%), United Kingdom (18%), Canada (18%), Germany (3%), the Netherlands (2%) and Australia (2%), n=39 'other' countries of origin were represented in the articles included for review. Table B.1 (follows) presents a summary of this information.

Table B. 1 'Other' countries of origin represented in articles included for review

	Magazine Articles	Newspaper Articles	Journal Articles	Reports	Total
Austria	-	-	n=2	n=1	**n=3**
Belgium	-	-	-	n=3	**n=3**
China	-	-	n=1	-	**n=1**
Denmark	-	-	n=2	-	**n=2**
Ireland		n=2	n=1		**n=3**
Italy	-	-	n=4	-	**n=4**
Japan	-	-	n=3	-	**n=3**
Korea	-	-	n=2	-	**n=2**
Spain	-	-	n=2	-	**n=2**
Sweden	-	-	n=3	-	**n=3**
Switzerland	-	-	n=2	n=3	**n=5**
Taiwan	-	-	n=3	-	**n=3**
France	n=1	-	-	-	**n=1**
Kenya	n=1	-	-	-	**n=1** **(Cont'd)**

TABLE B. 1 (CONT'D) 'OTHER' COUNTRIES OF ORIGIN REPRESENTED IN ARTICLES INCLUDED FOR REVIEW

	Magazine Articles	Newspaper Articles	Journal Articles	Reports	Total
Czech Republic	-	-	n=1	-	**n=1**
Hungary	-	-	n=1	-	**n=1**
Pakistan	-	n=1	-	-	**n=1**
TOTAL	**n=2**	**n=3**	**n=27**	**n=7**	**N=39**

B.2 'BIG OIL' AND SYNTHETIC BIOLOGY-BASED BIO-FUEL PRODUCTION

'Big oil' giants may have once considered alternative fuels a "bad investment" (493), however, in recent years, many have become increasingly interested in moving in a "green direction" to help fight global warming (303,494). Many have begun working with SB companies (Table B.2) to develop microbes to produce advanced bio-fuels, currently making this envisioned application area the most commercially funded of all other types. These companies have a natural affinity for the business of alternative energy because of the experience and expertise gained in the production and marketing of fossil fuels (307). Major motivations behind their increasing investment in SB-based biofuel production were mainly cited as dwindling oil supplies, stricter government regulation around greenhouse gas emissions (293), and the possibility of inexpensive, efficient, and scalable production (52,153,357,417)

TABLE B. 2 COMPANIES THAT USE SYNTHETIC BIOLOGY PLATFORMS TO CREATE BIO-FUELS

SB Company *(Location)*	SB Bio-fuel Research Initiatives

Amyris Biotechnologies *(Emeryville, California)* (254,310)	• Use a similar SB platform as that used to create Artemisinin
	• Currently working with oil giants **BP***, **Shell**, and **Total** to create synthetic yeast that produces enzymes capable of breaking down sugarcane
	    o This process produces farnesene (frangrant oil) that can be converted into diesel fuel
	    o Hope to create bio-jet fuel using similar processes in the future

LS9 *(South San Francisco, California)* (310,360,495-497)	• With an investment from **Chevron** LS9 is currently using SB techniques to modify *Clostridium phytofermentans* to convert plant matter to ethanol with high efficiency. • Fuel produced using this method is designed to float to the top of a fermentation tank for easy retrieval
Solazyme *(South San Francisco, California)* (316,498,499)	• Uses SB techniques to produce algal-based kerosene called "Soladiesel" o Suitable for use in jet engines (commercial and military). • Algae are naturally photosynthetic but this company grows the microbe in the dark, and thus, use fermentation instead of photosynthesis. • **Chevron** has reportedly partnered with Solazyme to help create Soladiesel
Synthetic Genomics *(La Jolla, California)* (203,254,438,500, 501)	• Aims to commercialize a range of SB applications; energy products are its first major target. • Partnered with oil giants **BP** and **ExxonMobil** to improve the biological conversion of fossil fuels into energy o *E.g.* organisms designed to convert natural gas from CO_2) (**BP**), and to develop and commercialize algal-based bio-fuel (**ExxonMobil**)

* BP has also been working with DuPont to develop bio-butanol since 2003 (496,502)

Apart from the companies listed in Table B.2, the United States' government has become particularly interested in the SB-based bio-energy business. The country's Department of Energy reportedly invested $12 million in the J. Craig Venter Institute for Biological Energy Alternatives in hopes that the scientist will find ways to use the energy of the sun and carbon dioxide to create bio-fuels (332). Further, the United States Military has reportedly expressed interest in using SB for energy production (28).

B.3 Advantages and Disadvantages of Conventionally-Produced Bio-Fuels

There are advantages and disadvantages associated with the production, and use, of all bio-fuels. Table B.3 provides a summary of select advantages and disadvantages of four bio-fuels commonly discussed across the literature scoped. Many points are identical to fuels produced using SB methods.

Table B. 3 Advantages and disadvantages of conventionally-produced bio-fuels

Advantages	Disadvantages
Bio-butanol: *Produced by microbial fermentation of plant-based starch (corn, sugar cane, beat cane) and simple sugars* (503,504)	
• More efficient than bio-ethanol, has a high energy content per weight (more favourable replacement for gasoline) • Non-corrosive; compatible with existing storage and transportation structures • Has low hygroscopicity (does not attract water molecules) and miscibility in water; distillation process less expensive than ethanol • Can be used directly in a traditional gasoline powered engine	• Produced in low yield • Difficult to purify, produces unwanted by-products during production • More toxic than ethanol, has an unpleasant smell • Produced using foodstuffs; presents a strain on food infrastructure (food ***vs.*** fuel) • Produces a fossil fuel when combusted (CO_2)
***Bio-ethanol*:** *Produced by microbial fermentation of plant-based starch (corn, sugar cane, beat cane) and simple sugars* (182,503,504)	
• Produced in high yields by naturally-existing organisms • Easy to produce using well-known and established processes (*e.g.* large-scale fermentative infrastructure already exists) • Can be used in 'flexible-fuel' vehicles	• Low energy density profile (30 percent less energy than gasoline); does not compare favourably to traditional gasoline 'gas mileage' • Corrosive; incompatible with existing storage and transportation structures (*e.g.* pipelines); automobile engines must be modified to use it • Hygroscopic and miscible in water; distillation process expensive • Produced using foodstuffs; presents a strain on food infrastructure (food ***vs.*** fuel): heavy agricultural burden (197) • Produces a fossil fuel when combusted (CO_2)
	(Cont'd)

TABLE B. 3 (CONT'D) ADVANTAGES AND DISADVANTAGES OF CONVENTIONALLY-PRODUCED BIO-FUELS

Advantages	Disadvantages
Bio-hydrogen: *Produced by photo-fermentation and bio-phytolosis of water* (504)	
• A 'clean-burning' fuel (produces water as a bi-product); does not contribute to global warming • Entirely non-toxic • Second highest energy density (per weight) of any fuel known today • Separates itself automatically from microbial culture	• Hydrogen infrastructure not yet in place (vehicles, storage, transport) • Fuel cells currently very expensive to make
Bio-diesel: *Produced by chemically reacting vegetable oil or animal fats (recycled restaurant grease)* (182,503,504)	
• High energy density • With minor modifications, compatible with existing petroleum-based automobiles	• Large-scale production difficult; enormous, almost unattainable, amounts of feedstock required to produce bio-diesel at industrial scale • Fatty-acids in bio-diesel lead to unfavourable effects on internal combustion engines • Produces a fossil fuel when combusted (CO_2)

B.4 THERAPEUTIC NATURE OF ENVISIONED HUMAN HEALTH PRODUCTS

Envisioned human health products were discussed in some detail across the literature analyzed in this review. Three broad types of products were identified: products that produce a medicinal chemical or other therapeutic substance for use in the body (Table B.4), those that act therapeutically within the body (Table B.5), and those that act therapeutically within the body and produce a medicinal chemical or other therapeutic substance (Table B.6). In the three tables that follow, each of the products identified is discussed in further detail.

TABLE B. 4 ENVISIONED SB PRODUCTS THAT PRODUCE A MEDICINAL CHEMICAL OR OTHER THERAPEUTIC SUBSTANCE FOR USE IN THE BODY

Type of Action & Product	Explanation
Objective: Prevention	
Viral and DNA based Vaccines (n=64) *E.g.:*(48,108,189,310, 330,372,385,410,505)	• DNA-based vaccines could also be more targeted toward specific pathogens • The creation of DNA-based vaccines could be streamlined • Vaccines to be created 'on-the-spot'; a perfect match to the genetic material of the actual pathogen. • The lag time for DNA-based vaccine creation could be reduced to weeks, instead of months or years; the genome of a potential influenza seed virus, for example, could be synthesized from scratch and placed in a specialized cell for faster replication. • First steps could be accelerated using computer modeling; could facilitate identification of virus strains and its unique genetic code against which the vaccine will be used.
Objective: Prevention and/or Treatment	
Production of Designer Protein Drugs' such as Therapeutic Monoclonal Antibodies (n=6) (48,83,304,344, 345,506)	• Described as "one of the most powerful" potential applications of SB • Through rational design, SB could allow the creation of novel designer protein-based therapies such as monoclonal antibodies, grown in less expensive designer microbes using synthetic genes. This could reduce the time needed to develop and produce them. • Antibodies could be synthetically engineered with enhanced half lives
Objective: Treatment	
Production of 'Natural' Pharmaceutical Products (n=4) (104,197,362,507)	• Microbial metabolic pathways could be re-designed to produce many types of pharmaceutically-relevant chemicals making the production of certain natural medicinal compounds cheaper. o *Eg*: Artemisinin (anti-malarial drug), shikimic acid (key precursor to anti-influenza drug Tamiflu), and taxol (used in anti-cancer chemotherapy)
Production of Antibiotics (n=14) (87,108,197,312,344, 345,353,358,362,370, 400,432,508,509)	• If new types of bacteria were identified for which no existing therapy existed, SB could shorten the time needed to develop a therapy by rationally designing antibiotic targets. For example, an antibiotic could be specifically made to combat the 'defences of resistant strains of bacteria' such as *C. difficile*. **(Cont'd)**

TABLE B. 4 (CONT'D) ENVISIONED SB PRODUCTS THAT PRODUCE A MEDICINAL CHEMICAL OR OTHER THERAPEUTIC SUBSTANCE FOR USE IN THE BODY

Type of Action & Product	Explanation
Objective: Treatment	

Production of Inexpensive Blood Substitute
(n=2)
(373,510)
	• The creation of a whole blood substitute could address several shortfalls:
	    o low number eligible donors: not everyone who needs blood receives blood,
	    o blood safety (especially non-Western countries).
	    o blood substitutes could be made to withstand longer storage times than blood obtained from another person, and
	    o although extensive testing is completed on blood received from donors, its entire content cannot be known

The Creation of Replacement Organs; Tissue Engineering & Regenerative Medicine (n=21) *E.g.:* (151,310,342,346, 350,357,511,512)	• Stem cells from those in need of an organ could be induced to differentiate into the desired organ • Organ rejection would be solved because the patient's own cells would be used to create the replacement organ

TABLE B. 5 ENVISIONED SB PRODUCTS THAT ACT THERAPEUTICALLY WITHIN THE BODY

Type of Action & Product	Explanation
Objective: Prevention	
Microbes designed to Enhance the Function of our Immune System (n=5) (108,151,334,344, 345)	• Bacteria, ingested as a single pill, could be designed to circulate through the bloodstream as an extension of our natural immune system. Several functions could be performed by these bacteria, such as providing our bodies with vitamins and performing other immune reactions, as required • Immune cells could be engineered to become more efficient at detecting viruses and bacteria than our 'regular' immune systems. • This might allow us to combat novel infectious diseases or bacteria that have become resistant to antibiotics
Detection and Neutralization of Toxins (Primarily in Water) (n=7) (28,88,108,169, 357,417,424)	• Bacterial biosensors could be engineered to detect and/or neutralize toxins in drinking water (*e.g.* arsenic) • bacterial genes could be engineered to glow, or produce acid, if a toxin is detected allowing visual detection or detection through inexpensive pH testing devices
Objective: Prevention and/or Treatment	
Treating Genetic Disorders: Gene Therapy and RNA Silencing (anti-sense and RNAi)- using Nucleic Acid Drugs and Personalized Medicine (n=16) (49,106,139,151,153, 197,319,321,344,381, 511,513-517)	• SB could offer a more controlled approach to gene therapy, making it possible to create and administer exact matches of 'corrected' patient chromosomes using bacteria or viruses as gene delivery vectors. Modified nucleic acids could be created and mass-produced for use in genetic therapy far more economically than conventional approaches.
Robot Surgeons: Disease Detection and/or Treatment (n=6) (151,188,344,357, 380,454)	• Robot surgeons could be designed to circulate our bodies to detect, and/or treat a variety of diseases, and damaged tissue, before they become severe. • Could enable quick detection, localization, and destruction of tumours. This would allow faster treatment and, ultimately, increase the patient's chances of survival. • For a disease like cancer, *in vivo* cell counters could be designed to keep track of the number of times cells divide, detecting and alerting the patient to out of control cell division • To alert patients of problems, 'biosensors' could be engineered to emit detectable wavelengths based on conditions sensed. **(Cont'd)**

TABLE B. 5 (CONT'D) ENVISIONED SB PRODUCTS THAT ACT THERAPEUTICALLY WITHIN THE BODY

Type of Action & Product	Explanation
Objective: Treatment	
Bacteria and Bacteriophage Drug Delivery Systems & 'Smart Drugs' (n=16) (49,52,106,130,139, 151,153,197,200, 242,329,344,421, 513,518,519)	• Given that bacteriophage are species-specific, they could be: ○ designed to deliver therapeutic proteins or anti-microbial peptides to infectious organisms in a highly specific manner; engineered as antibiotic adjuvants • Targeted delivery of anti-bacterial medication would, for example, allow for the efficient treatment of the bacterial infection while sparing mutualistic (beneficial) bacteria
Microbes that can Penetrate Biofilms (n=2) (197,425)	• Bacteriophage could be engineered to express biofilm degrading enzymes that attack biofilm infections within the body

TABLE B. 6 ENVISIONED SB PRODUCTS THAT ACT THERAPEUTICALLY WITHIN THE BODY AND PRODUCE A MEDICINAL CHEMICAL OR OTHER THERAPEUTIC SUBSTANCE

Type of Action & Product	Explanation
Objective: Prevention and/or Treatment	
Detecting and Treating Viral Infections, Especially HIV (n=8) (52,53,87,319, 330,337,505,520)	• A living therapeutic device could be engineered to circulate through the bloodstream for the purpose of recognizing, and respond to, HIV activity o The device could be engineered to produce an anti-viral immediately upon HIV detection to stop the further spread of infection • Prostratin is a promising chemical undergoing clinical testing for the treatment of HIV infection, but is currently only found in an uncommon plant called '*Homalanthus nutans*'. SB could be used to produce this promising chemical in unlimited quantities.
Cancer Treatment: Locating and Killing Tumours (n=53) *E.g.* (87,104,242,323, 325,351,400,412, 506,521,522)	• Microbes and viruses could be engineered to target specific tumours; toxic molecules could be used on cancer cells without negative systemic effects • **Microbes**, the 'perfect' anticancer agents(188) , could be designed to permanently reside in the body and recognize hypoxia, a "telltale sign of cancer tumours", amass around them, and release a toxin that is deadly to tumour cells. o An active therapy, such as self-propelled microbes, would allow tumour penetration not accessible to passive therapies. • **Viruses** could be designed to permanently reside in the body and identify, kill, cancer cells • The human virus AAV2, known to selectively kill a variety of cancer cell lines could be synthetically engineered to create a useful virus-based anti-cancer therapy
Microbes Engineered to Detect and Dissolve Dangerous Substances that Accumulate in Our Bodies (n=1) (407)	• Microbes could be designed to travel through our bodies and detect dangerous substances and digest them before clinical symptoms are realized o *E.g.* detect and digest fatty deposits on artery walls
Objective: Treatment	
Molecules that Analyze the Intercellular State Prior to Delivering a Therapeutic Effect (Controlled Delivery) (n=1) (407)	• DNA-based sensors could be designed to circulate throughout our bodies and analyze the state of our cells prior to delivering a therapeutic effect (*e.g.* an antibiotic) o could be used to control the directed release of drugs to specific areas in the body and ensure that drugs are only delivered to specific cellular targets when they are needed • The controlled release of drugs could lead to a reduction in unwanted side effects

TABLE B. 6 (CONT'D) ENVISIONED SB PRODUCTS THAT ACT THERAPEUTICALLY WITHIN THE BODY AND PRODUCE A MEDICINAL CHEMICAL OR OTHER THERAPEUTIC SUBSTANCE

Type of Action & Product	Explanation
Objective: Treatment	
Internal Biosensing Devices that Recognize when a Drug is Administered (n=1) (330)	• Specialized bio-sensors could be built to recognize when a drug has been administered • Once the drug is recognized a circuit would be established with the immune system, telling it either a) to act upon unhealthy cells or b) to recognize a disease biomarker and release an appropriate drug when the marker is detected
Type I, II Diabetes Treatment/ Management: Automatic Creation of Beta Cells and Cells that Monitor Insulin Levels (n=7) (40,48,49,52, 319,406,416)	• Autoimmune attacks in Type I diabetes could be managed by engineering stem cells to help the body maintain synthetic homeostasis • Stem cells could be engineered to monitor the number of beta (insulin-producing) cells. When the number drops below a defined threshold, they would be designed to divide and differentiate to create additional beta cells • Engineered cells could be engineered to monitor the level of insulin within the body o When the system detects insulin levels below a prescribed threshold concentration, insulin would be synthesized and secreted in the blood • A regulatory circuit could be designed to synchronise with body's natural circadian rhythm and trigger the production of insulin as needed

B.5 Social Risks and Concerns of Synthetic Biology

Table B. 7 Numerical breakdown of articles that mentioned or discussed risks related to SB and its envisioned products

	Newspaper Articles (n=155)	**Magazine Articles (n=90)**	**Journal Articles (n=96)**	**Reports (n=26)**	**Total (n=367)**
General					
All Risks	n=91 (59%)	n=38 (42%)	n=35 (36%)	n=26 (100%)	**n=190 (52%)**
Physical: Bio-security					
Engineering Antibiotic Resistant Microbes	n=5 (3%)	n=0	n=0	n=4 (15%)	**n=9 (2%)**
Bio-Terrorism	n=52 (34%)	n=22 (24%)	n=13 (14%)	n=21 (81%)	**n=108 (29%)**
Dual-Use	n=3 (2%)	n=5 (6%)	n=7 (7%)	n=12 (46%)	**n=27 (7%)**
Physical: Bio-safety					
Accidental Escape	n=13 (8%)	n=3 (3%)	n=1 (1%)	n=11 (42%)	**n=28 (8%)**
Physical: Environmental					
Environmental	n=0	n=15 (17%)	n=14 (15%)	n=22 (85%)	**n=51 (14%)**
Non-physical: Ethical and Intellectual Property					
Ethical Concerns	n=49 (32%)	n=26 (29%)	n=27 (28%)	n=26 (100%)	**n=128 (35%)**
Intellectual Property	n=21 (14%)	n=14 (16%)	n=12 (13%)	n=26 (100%)	**n=73 (20%)**