Comments on the draft documentation on new and emerging issues – deadline 20 September 2013

New and emerging issues relating to the conservation and sustainable use of biodiversity - potential positive and negative impacts of components, organisms and products resulting from synthetic biology techniques on the conservation and sustainable use of biodiversity

Potential Positive and Negative Impacts

Page	Line	Comment
4	Box 1	The definition of Synthetic Biology should be limited to processes or organisms that involve the use of nucleic acids that are produced by *de novo* synthesis, and not encompass all of genetic engineering and/or classical genetics.
9	35	ii) Products from synthetic biology – the examples cited in the following pages are in many cases not from synthetic biology, but from "standard old-fashioned genetic engineering".
10	16	For example, Myriant's bio-succinic acid is produced by an organism that contains no foreign DNA and was generated by standard techniques of gene deletion and selection for faster growing natural mutants. No "Synthetic Biology" was used.
10	22	Robotic High-Throughput screening is frequently used in connection with Classical Genetics and Breeding. It can also be used in connection with Synthetic Biology (SB), but products can be developed with robotic High-Throughput screening which have nothing to do with SB. While robotic High-Throughput screening, DNA sequencing, or bioinformatics can all be considered as "synthetic biology tools", the use of these standard techniques does not necessarily imply that outcome is from SB, as the tools have other uses is classical biology.
12	28	The authors discuss possible unintended impacts caused by the survival and persistence of synthetically-modified organisms (SMOs). In a footnote, they indicate that no attempt is made to distinguish between a synthetically modified organism or a genetically modified organism (GMO). We believe organisms, and their products, should be evaluated with regard to their potential impact on biodiversity without regard to any particular technology used to modify the organism. It is well documented that natural (unmodified) organisms can have a dramatic negative impact on biodiversity when released into the environment (consider rabbits released intentionally in Australia or Zebra Mussels unintentionally introduced into the Great Lakes in the U.S.). In contrast, certain organisms intentionally released into the environment, in an effort to detoxify chemicals, have not had their intended impact due to a failure of the organism to persist in the environment. The potential impact of a released organism needs to be evaluated independent of whether it was modified using "synthetic biology", or any other technology. The potential impact is independent of whether the organism was modified, and is independent of which

		particular technology was used to modify a released modified organism.
12	29	The parenthetical inclusion of biosafety is grammatically ambiguous. It the statement intending to subsume biosafety into the definition of biodiversity? Or is it intended to suggest that the encapsulation of the three broad categories of unintended impacts are in general biosafety considerations?
12	29-30 and footnote #27	The inclusion of the terms synthetic organism and synthetically-modified organisms (SMO), plus modified microorgansisms (SMMOs) is not coherent with the usage in the Marris and Jefferson (2013) citation itself. Though while the authors note its emergence, they *do not propagate its usage even in their own report*. They indicate that for risk regulation one should observe the terminology within the respective national regulatory vocabulary. Even within this CBD, other documents indicate challenges of defining the CBD's own terms (LMO) so the inclusion of SM(M)O terminology is unjustified.
12	33-34	The report indicates that positive impact could be had, and likewise negative, but subheading *i)* focuses <u>only on the authors self-categorized negative impacts</u>. There nowhere appears a subheading here clearly focusing on positive impacts. *ii)* transitions to unintended release, *iii)* to intentional release and there appears no follow on section
12	40ff al of section *i)*	The paper fails to note that Wright et al. 2013, which is incorporated in its footnotes, states "[t]hese concerns echo old questions raised previously by the introduction of recombinant DNA technology". What is not established is a rationale for what makes this discussion different. For instance, see next comment.
13	1	The authors cite potential pollution from engineered algae that produce oils, or from plants that produce enzymes, such as cellulases, that lead to breakdown of the plant biomass once its harvested. In this example, the authors are focusing on traits of the organism, rather than on the technology used to produce it. We feel this is the right approach. The authors mention the potential of "algal blooms" from escaped engineered algae, which were developed to produce bio-fuel. It's unclear why engineered algae are more likely than natural algae to create algal blooms? Natural algal blooms, in response to chemicals such as phosphates, are well documented. It's unclear why escaped engineered algae, in particular, are likely to contribute to increased algal blooms.
13	7	It is true that SMO's cannot be retrieved once released, but neither can any living organism—regardless of the technology used to modify it. From this perspective the organism must be evaluated based on judgment regarding its ability to be invasive. There is no reason to believe an organism will be more invasive simply because it was produced using synthetic biology. We feel that potential "invasiveness" is a property of the organism that is being manipulated, and is not a function of the technology used to manipulate the organism. From that perspective, consider that that the food and beverage sector has been using, and modifying, various yeasts and bacteria (including *Saccharomyces* and

		Bacillus) for 10,000 years and these species have not invaded the natural environment and reduced biodiversity. In addition, processes aimed at inactivating microorganisms used for industrial scale-production have been shown to work. For example, Novozymes uses a process to convert microorganism into fertilizer and published studies aimed at detecting the organisms, or any of its genetic material, in fields post-application of the fertilizer failed to detect the organism or its DNA. In this case, the bio-product is being manufactured and sold, and the engineered microorganism is not over-running the environment (Moller et al., Res. Microbiol. 152 (2001) 823-833).
13	8	The authors argue there is little baseline data for many of the organisms being transformed by SB on interactions in the natural habitat. In the absence of specific examples, it is impossible to comment on this general statement. However, it might be reasonable to place organism with a long history of safe use (*Saccharomyces*, *Bacillus* and others) in one category from the perspective of concern regarding potential environmental impact and to place other organisms in another category; and to expect an environmental impact study be conducted prior to initiating engineering of organisms in the second category. We agree with the concluding statement of the paragraph: "the results of current SB research and commercialization (ie, not yet orthogonal systems such as xenobiology) are sufficiently "familiar" that risk assessment checklists for conventional GMOs are still appropriate (de Lorenzo 2010)."
13	11-12 & 15-16	A point is made that "SB organisms are living and reproducing, however, they can evolve". This is likewise true of the organisms contrasted in the preceding sentence. This is an emotional appeal, not a scientific argument. This is precisely the same issue with the concluding sentence that SMO's cannot be retrieved once released.
13	18-19	This statement is seemingly disingenuous when contrasted with the footnoot #27. In bold font this section argues to **"disagreement over adequacy…of conventional GMO risk assessment methodologies to SMOs."** While footnote 27 states " The use of these terms does not indicate a position on whether these organisms are different from genetically-modified organisms (GMOs) or genetically-modified micro-organisms (GMMOs)." Introduce a term, bury it in a footnote, use it in a way not used by the cited authors, then use a bolded heading which argues for a difference between the terms.
13	32	This paragraph discusses the potential of gene transfer from engineered organisms to natural organisms. It is true that horizontal transfer can occur and that engineered genes have the potential to move into natural species where they might persist due either to selection for traits the genes encode, or the genes might persist due simply to random genetic drift. Although it can be argued that gene transfer might represent a danger to biodiversity, there is no compelling reason to assume horizontal transfer of engineered genes is a threat to biodiversity. The benefits to society derived from bio-engineering need to be weighed against the potential, but unknown and unproven, negative impact of

		gene transfer.
13	49	The authors describe the concept of “genetic pollution”, suggesting that horizontal transfer of genes is, in and of itself, harmful, even if no particular negative effects are caused by the transferred genes. We do not feel horizontal transfer of genes is, by definition, “harm”.
13	51	Spread of antibiotic markers, again there is no argument made as to why this is a new and emerging issue, or exacerbated by “synthetic biology”. Nonetheless, see next point.
14	2-3	While making no argument about the merits of antibiotic resistance being a substantively different HGT issue in synthetic biology, they then argue it doesn’t matter, because just the spread of ‘synthetically designed DNA’ is an issue, so called genetic pollution. This section relishes in the euphemism of ‘pollution’ and thereby does not appear to deal seriously with its own citation (Marris and Jefferson 2013) “…assuming that the horizontal transfer of genetic material is, in itself, the important adverse effect that needs to be prevented. Interestingly, synthetic biologists share this view with environmental NGOs who are critical of genetic engineering and of synthetic biology, and both groups use terms such as “genetic pollution” and “genetic contamination” to describe this phenomenon. **But the perspective of regulators and scientific experts involved in environmental risk assessment is rather different: in these circles, gene transfer is not understood as a hazard or adverse effect in itself; what matters is the identification of adverse effects that might occur as a result of the transfer of genetic material**.” (emphasis added) To have a serious discussion on this topic we must extract ourselves from the mindset of regulation by metaphor.
14	11	We feel the discussion misses the point by focusing on possible negative emergent properties of organisms modified via synthetic biology (SB). Non-native organisms can potentially cause harm when introduced into a particular ecosystem—whether the organisms are engineered or not. The argument made here is that because the organism was engineered using “new to nature” designs, it is possible that the organism might express some unpredicted emergent negative phenotype. This, in theory, is possible, but the risk needs to be examined and considered on a case-by-case basis. A possible extension of the argument made in this paragraph is that synthetic biology research should be conducted with a high level of containment because it is possible that an organism that displays an unanticipated and harmful phenotype might be developed. This level of precaution will slow progress in the field and might result in a failure to develop products that could provide significant benefit to society.
14	11-21	While the paper cites extensively Schmidt and de Lorenzo 2012 to point out unpredictable and emergent properties, they fail to note that “[n]ew and emerging technologies, described as having a major impact on society, are frequently accompanied by a rhetoric firework of hope, hype and fear. Synthetic Biology, openly declaring the pursuit of a scientific and technological agenda that tries to overcome the natural state of affairs, is no

		exception. But despite the new language and the fresh metaphors that surround SB, many questions on safety and security of microorganisms bearing synthetic genomes have been raised before in connection to Genetic Engineering.”
14	23	This paragraph describes an experiment that led to the development of a mousepox virus, designed to induce infertility, which instead was highly lethal to mice. The authors rightly note that the engineered virus was produced using standard recombinant DNA techniques. This example illustrates that products of bio-engineering need to be evaluated carefully and thoughtfully, regardless of the name assigned to the technology used to create the products.
14	32	The authors reference writing of Rees and others, particularly noting that Rees indicates that synthetic biology is a potential existential threat that could cause “worldwide devastation”. In his Science editorial, Rees mentions several other existential threats, including the possibility that the World’s extensive and complex computer network might become self-aware. Risks of this sort fall into the category of “unknown unknowns”. These risks need to be considered in contrast to a vision of a world that lacks computers or biotechnology. Computer science and biotechnology are key technologies that provide us with an opportunity to understand and manage the greatest problems in the World today. Considering bio-science in particular, the technology will enable us to generate more food using less land and water resources, and will also solve problems in the health and environmental sectors. Whether synthetic biology will destroy the human species is unknown, but seems unlikely. However, human society, and biodiversity, will certainly be harmed if biotechnology is not used to confront the major problems of our time. We believe that SB allows the only effective and potentially rapid enough route to transition from a fossil based economy to a biobased one, and perhaps slow & stabilize global climate impacts by utilizing carbon dioxide, natures original feedstock, for the production of renewable chemicals and biofuels.
14	32-36	And likewise other philosophers have concluded that, “[i]n the final section I will make the case with regard to human existence, arguing that synthetic biology, even if wildly successful, is not in a position to cause significant existential change in what it is to be human over and above the massive existential change caused by the transition to agriculture.” Preston, B. (2013) Synthetic biology as red herring. Studies in History and Philosophy of Science Part C: Studies in History and Philosophy of Biological and Biomedical Sciences, http://dx.doi.org/10.1016/j.shpsc.2013.05.012
15	8-9	In what discipline of science is any series of controls “never fail-proof”? Is this a relevant, if even achievable, standard?
15	11-13	While quoting Schmidt and de Lorenzo on the sensational side (organisms have escaped, and massively), they fail to further acknowledge the subsequent context of their argument. “Yet, these *(note’ these’ refers to the antecedent ‘massive’ escapes, comment inserted)* are

		somewhat minor occurrences compared to the worst-case scenarios that were predicted during the onset of the cognate technologies 40 years ago [9]. That no engineered microbe has even been traced to any disease or has caused any detectable problem is an indicator that safety measures have so far been sufficient (or that forensic methods to this end have worked poorly). In contrast, natural pathogens occasionally escape the laboratory and cause diseases [10–13]." This section amounts to selective quotation for sensational effect.
15	26	Physical containment is discussed in this section. The "precautionary principle" is mentioned, suggesting that all synthetic biology work should be conducted at a high level of physical, geographic and biological containment. Our perspective is that organisms, whether natural or engineered, need to be contained based on an assessment of the danger of the organism. This is the approach that has been followed with regard to regulation in the United States, and we feel this approach should be followed going forward.
15	28	Requiring all organisms containing synthetic DNA to be studied under Biosafety Level 3 or even 4 conditions would inhibit most current genetic engineering, including traditional genetic engineering that does not involve any "new-to-nature" gene designs.
15	16-35	While once again citing abundant work supporting a stance on moratorium, the document leaves with a single citation to the counter. This fails to acknowledge that the Presidential Commission for the Study of Bioethical Issues " found no reason to endorse additional federal regulations or a moratorium on work in this field at this time." Furthermore it specifically examined the suggestion to adopt an extreme 'precautionary principle'. " The principle of responsible stewardship rejects two extreme approaches: an extreme action-oriented approach that pursues technological progress without limits or due regard for public or environmental safety, and an extreme precautionary approach that blocks technological progress until all possible risks are known and neutralized."
15	37	The authors discuss strategies for biological containment including "kill switches" that will inactive an organism once it leaves a specific environment; horizontal gene transfer prevention; trophic containment; and semantic containment. The need to use features of this sort during engineering of an organism is a function of the level of danger associated with the particular organism. Even "safe" host organism can mutate and evolve. Biosafety considerations should be engineered into any modified microorganism that might have the ability to proliferate in the environment with negative consequences, such as renewable chemical organism. After all, we don't want oceans or lakes full of renewable chemicals that don't belong there, just as we want to avoid water pollution via inorganic chemicals. When BL1 organisms that are GRAS are manipulated, these features are not necessary, unless genes will be introduced into the organism encoding products (such as toxins) that result in assignment of the engineered organism to a higher risk category (BL2 through BL4).

15	40	Once again, as with comments on page 13, lines 18-19 above, the document reverses it's stated position not to make judgments on the merits of GMO versus SMO, and introduced that term for purposes of exactly that. Line 40 argues that understanding fitness from the past experience of GM's will need a different standard for the SMO. Moreover the 'built in safety features' proposed for SMOs are no different than those proposed in the past for GMOs.
16	16-18	This represents another example of incomplete dealing with an underlying citation. Moe-Behrens is represented "note that few of the genetic, safeguards, including engineered autotrophy, can meet the recommended limit…", however, they actually state "So far, only a few of the genetic safeguards meet this limit." Furthermore, despite a 2013 publication date, Figure 2 cites no example later than 2006, with the average date listed being 1995.
17	10	This section discusses societal aspects of containment. The modern biotechnology industry has focused on bio-safety, as exemplified by the early Asilomar Conference on Recombinant DNA, from its inception. Individuals trained in traditional settings receive standard instruction on the safe practice of recombinant DNA technology. Furthermore, the detailed nature of the instruction is a function of the characteristics of the particular organism being manipulated (BL1 through BL4). Today, given the advent of trends such as *Do it Yourself Biology* (DIY) people are entering the field who have not been exposed to the traditional biosafety and laboratory training. From the perspectives of health and human safety, and also with regard to unintended or intended release of organisms into the environment, we feel it is important that all practitioners are following the same fundamental guidelines. We feel that all practitioners (including single individuals working alone) should be required to notify a local authority that they are practicing bio-engineering of any sort (including traditional mutagenesis, recombinant DNA technology, synthetic biology, or whatever). In the U.S., issues such as the level of containment and practices regarding the proper disposal of biological waste should conform to local regulations. However, over time, we feel an effort should be made to standardize these regulations (for example implement regulation similar to the NIH Guidelines) so that (*although the oversight and authority is local) all practitioners are following the same set of guidelines, and are handling material in the same manner, regardless of their geographic location; and without regard to whether they are working at an academic institution, a for-profit-company or a DIY facility.
17	21-24	Cites iGEM as an example of a situation where synthetic biologists are too early in their career to be familiar with the lab, as reason to question social aspects of containment. Yet, they fail to mention the over aspects of biosecurity and biosafety *required* as a component of each team's entry. The iGEM competition has had a longstanding relationship with the FBI regarding the responsibilities of working in this new field
18	2, 10-17	This is yet another example of the divisive use of the SMO label. What organisms are in *use* now? GMOs or SMOs? And how is this need, say bioremediation, manifestly different

		than that need in the 1980's? This does not reflect a NEW issue. Confusing and misinterpreted definitions and labels can be very problematic and result in ineffective and over burdensome regulations.
18	10	The authors wrongly state that Modular Genetics, Inc. (Modular) is developing organisms that will be release into the environment to clean up oil spills. In particular, Modular's surfactant program is mentioned in a section entitled: *Intentional release of synthetically-modified micro-organisms (SMMOs)*. The company has developed engineered microorganisms that produce surfactants and it has been shown that, from a performance perspective, these bio-surfactants can be used to replace dispersants that were of concern during the BP oil spill (I.e., COREXIT). Modular's surfactants might be used in the future for oil spill remediation. The surfactants are produced at a production facility, and are purified to a high level of purity using "green" purification methods. The purified surfactants do not contain microorganisms, or microorganism components (other than the purified bio-surfactant). We believe it is important for groups to interact with the proper regulatory agency (e.g., EPA, USDA) to gain clearance prior to any intentional environmental release of an engineered microorganism. We believe the regulations and processes in place to manage these releases are sufficient to regulate organisms generated using any current bio-engineering method, including synthetic biology. An organism should be regulated based on a judgment regarding its risk as an organism. It should not be regulated based on whether it was produced using a particular technology, including synthetic biology. Consider this example. Most engineered isolates of *Clostridium botulinum* are dangerous, whether or not "synthetic biology" was used to modify them. Most engineered isolates of *Bacillus subtilis* are safe, regardless of whether synthetic biology was used to modify them. We need to regulate products rather than technologies.
18	42-48	And, these products will proceed through regulatory and risk assessment channels.
18	43	While mentioning new company Agrivida who reportedly uses "a novel approach to synthetic biology" to engineer plants, there is no mention of major seed companies such as Monsanto, or Pioneer(Dupont), or BASF, etc., who have used traditional genetic engineering, and presumably more recently SB to engineer most of the corn, soybean, and cotton planted in the USA.
19	5	This section of the document discusses use of biological techniques to potentially "bring back" extinct species. A group called Frozen Ark has been collecting DNA and tissue samples from extinct and near extinct species since 1996. Given that DNA provides the blueprint for development of an organism, it should be possible, in certain cases, to regenerate living examples of currently extinct creatures. From the perspective of maximizing biodiversity, this technology is appealing since it offers hope for reproduction of species even after they have been driven to extinction. The rationale for seeking to restore

		one species relative to another will be the subject of much debate. In addition, it is unclear how the work will be funded. It is our view that it is prudent to collect genetic material from endangered species so that it is available in the event it becomes desirable to seek to restore the species—if so, the material would be collected and stored as a form of "insurance". On the other hand, we feel it is better to devote resources, including investment in the field of synthetic biology, to programs with the potential to dramatically slow the rate of loss existing species in order to avoid reaching a point where "synthetic biology" is the only path forward for restoring a sustainable global eco-system. In other words, we feel resources are best spent on seeking to conserve species that are not yet extinct, rather than seeking to restore extinct species. From a strictly financial perspective, it is likely that funding that might lead to the restoration of a single extinct species could be deployed in a manner that it instead leads to the conservation of thousands of species in a particular natural ecosystem.
20	4	Regarding bioterror and its potential impact on biodiversity, we feel it is important that all reasonable political means be used to block research and development on use of bio-weapons—whether they are targeted to human populations, livestock or crop species.
20	5-8	While the comparators make good phonetics, the underlying emergent issue or differentiation from any other technology impact is simply not presented. *Any* organism used for bioterrorism purposes *could* impact biodiversity. In the past 40 years have we not progressed past word games?
20	13-16	It continues to be disheartening to see disagreement or divergence of opinion manifesting itself as a "new and emerging issue". The comment states that one group sees this, and another sees that. But there is no articulation of what makes this an emerging issue *in or about synthetic biology*. As stated by Schmidt and DeLorenzo 2012 in the document's citation, "[n]ew and emerging technologies, described as having a major impact on society, are frequently accompanied by a rhetoric firework of hope, hype and fear. Synthetic Biology, openly declaring the pursuit of a scientific and technological agenda that tries to overcome the natural state of affairs, is no exception. But despite the new language and the fresh metaphors that surround SB, many questions on safety and security of microorganisms bearing synthetic genomes have been raised before in connection to Genetic Engineering."
20	36	Describes various perspectives on the future impact of synthetic biology on biodiversity and conservation. Our view is that it's clear that humans in general seek to control the environment immediately around them, for example by building shelters, raising livestock and growing crop species. We feel these activities are essential and we feel it is likely humans will continue to behave in this manner. In contrast to this tendency to manage and control their local environment, we feel that many humans recognize the value of conserving land in its wild and unmanaged state. We are optimistic that humans will reach a balance where it is understood that certain regions of the earth need to remain wild and

		untouched and we feel people should not seek to intervene and control the biodiversity in these natural areas. From that perspective, what role does synthetic biology have to play in maintaining biodiversity? If synthetic biology is used: to enable us to get maximal agricultural production from farmed land, to replace all of the commercially manufactured chemicals in use today with natural biodegradable chemicals produced using fermentation to convert underutilized agricultural material into chemical products, to generate carbon neutral transportation fuels and to develop bio-conversion technologies to clean-up the toxic chemical waste sites created via use of our historical technologies, then we will live in a cleaner, safer environment. Furthermore, manufacturing and consumption will no longer have a dramatic negative impact on climate change, which will create benefit for species such as polar bears, coral, and many others. In addition, there will be less incentive to clear rain forest to expand palm plantations because oils derived through biotechnology will eliminate the need for palm oil. It is our view that "synthetic biology" (and biotechnology in general) offers the opportunity for a complete replacement of the chemicals, materials and liquid fuels used today with renewable chemicals that are safer and carbon neutral. The efficient application of biotechnology, along with an effort to conserve large tracts of land in its natural state, should enable a high quality of life for the human population along with conservation of biodiversity. We are unaware of any other technology that has the potential to fundamentally change the way we make and use chemicals, materials and fuels so that "industrialized society" no longer generates toxic waste and destroys the natural environment. It is not reasonable to assume that all cases of horizontal transfer of engineered genes into natural species will be problematic. It is probably reasonable to assume that if the initial engineered organism itself is not a threat to biodiversity, particular subsets of its genes are probably not. From the perspective of the organism, or product, itself, and not from the perspective of the technology used to generate the organism. It is our view that modified organisms that have been generated by man, starting with the domestication of wolves to create dogs thousands of years ago, are part of the natural system given that they are derived from the natural system and operate at the molecule level in the same fundamental manner as "natural" organisms. From that perspective, they are living modified organisms. Or, perhaps more precisely, "Modified Living Organisms. "
22	48	The trade-offs between health outcomes and economic development to which the author here refers are common to many development scenarios and are not (and cannot fairly be characterized as) unique to SB. Indeed, the dilemma postulated by the author arises in virtually the identical way even in "old tech" agricultural development models. By way of illustration, the 12 March 2013 edition of the Maravi Post (Malawi) reported comments by Malawian President Joyce Banda characterizing the Framework Convention on Tobacco Control (the World Health Organization's anti-smoking campaign) as a "serious threat" to Malawi's economic progress because the Convention would restrict the supply and demand of tobacco products. Mrs. Banda stated that Malawi will continue to produce tobacco "until there is no demand." Mrs. Banda's reasons are evident: tobacco exports

		will generate more than $350M in foreign exchange for Malawi in 2013, representing approximately 53% of Malawi's total exports; more than half of Malawi's population has some involvement in the tobacco industry; and tobacco is responsible for approximately 80% of Malawi's total revenues. Clearly, progress in smoking prevention, which would greatly improve global health, could be catastrophic for Malawians, more than half of whom already live below the poverty line. The synthetic artemisinin example discussed by the author presents markedly similar issues of the difficult choices that often must be made between improved global health outcomes and the economic well-being of small agricultural producers and developing agrarian economies. For the author to imply that these complex issues emerge uniquely from advances in SB is inaccurate and overly simplistic. That does not mean we should shy away from grappling with these difficult questions, but it does suggest that SB should neither be singled out nor demonized as uniquely impactful in this regard.
25	1-7 & 22-33	While making a SynBio virus may be of some concern, the author comments indicate that SynBio will issue in a whole new range of pathogens is over blown. First nothing is better than a "natural" pathogen or agent, which already has been demonstrated to be easily used as a terrorist threat, e.g. ricin, anthrax. Second, while it is possible to synthetically make a whole bacterial genome, it is another matter to introduce it into a cell and assume that it will perform as designed. Also it is a bit naïve of the authors to suppose that a SynBio microbial cell will have a selective advantage over native microbes.
26	17-22	Persons with just technical skills will be able to make new bioweapons is erroneous – high level expertise in microbial physiology, genetics, etc. will still be need for SynBio research. SB technology provides new potential tools to create biosafe organisms with internal self-destruct mechanisms as well as new biosafety protocols.
27	21-32	The authors fail to mention that self-regulations were a basis of gov't regulation of genetic engineering that were instituted in the late 70's and early 80's (e.g. NIH Recombinant DNA Guidelines), which are enforceable through loss of grant money. Rouge organizations with questionable agendas will always exist, better to have the tools available to rapidly counteract a possible bio-threat
28-29	29-38 and 1-7	As for economic considerations: the bioeconomy began at the dawn of humankind through fermentation of wheat to beer, milk to yogurt, and grapes to wine. So the "bioeconomy" has been with us for a very long time. More recently, however, considerable benefit has been garnered from simple modifications such as engineered enzymes and the use of common, well understood organisms to produce new compounds via the insertion of synthetic genes copied from difficult to culture organisms.
29	17-30	Humans have been re-engineering their environment since the beginnings of agriculture. It is difficult to know if our gathering forefathers over grazed and drove to extinction any species. We are sensitive to the failures of mono-culture and to think that a single plant can be engineered to be commercially viable in all regions of the world is minimalizing the

		complexity of such an endeavor. It may be better to engineer plants for the environment in which they will be grown.
29	34	The term “Civil Society groups” been used to label NGO’s that have expressed concerns against SynBio. Would I suppose that a NGO that is for SynBio or does not have a concern be called a “Uncivil Society Group”? Such terms should be avoided by the authors or it may sound like “Newspeak”.