Written submission from the American University of Sovereign Nations (ENB0010)

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Introduction

This report has not attempted to address all the questions raised by the House of Lords Science and Technology Committee call for evidence on engineering biology. The main questions have been subdivided into supplementary questions identified as a, b, c etc and further subdivisions of i, ii, iii etc. The responses reflect our personal areas of knowledge and expertise, to assist the committee with some international insights from some different cultures into synthetic biology applications and bioethical considerations. With global trade and security facing new challenges and an ever changing population in the UK it is important to see new opportunities and seek ways to embrace new technologies in safe and morally acceptable ways. A lack of understanding regarding genetic engineering, by the general public, has been in part one reason for a reluctance to accept genetically modified foods in Europe and the UK. There is a need for fully transparent research and policy development to limit the spread of misinformation as was seen regarding vaccine development during the recent covid pandemic.

2. What are the key applications for engineering biology?

Engineering biology applies to a wide range of fields, which can be broadly categorised such as:

- Agriculture and food
- Medicines and health
- Materials and chemicals
- Renewable fuels
- Environmental applications including carbon cycling

a. i) Can you give examples of particularly exciting or interesting applications?

<u>Agriculture and food</u>

There is a plethora of examples of genetic engineering being used in over thirty countries (by more than 17 million farmers utilising 190 million hectares globally in 2019) to improve the agricultural production of crops (FAO, 2022b). These include maize, wheat, sugar beet, oilseed rape and many more, often by the inclusion of genes conferring disease resistance or to improve tolerance to herbicides and certain environmental conditions such as described by Kokhar *et al* (2023). Comprehensive reviews of genetically engineered crops for optimal and sustainable food production are given by Aziz *et al* (2022) and Sharma *et al* (2022) who explain how CRISPR/Cas9 gene editing and other technologies have been used towards achieving some Sustainable Development Goals by increasing tolerance to abiotic and biotic stressors, improving yields, quality and nutritional content and overall food security. Furthermore, as land for agriculture becomes increasingly limited and as climatic conditions become less conducive to achieving optimum yields the development of foodstuffs from biosynthetic cellular fermentations is becoming an increasingly viable alternative. Hilgendorf *et al* (2024) argue how precision fermentation has the potential to improve the flavour, quality, sustainability and safety of some food ingredients and nutrients. A selection of examples includes:

- An FAO (2022a) report cites several potential developments, which illustrate how some other countries are embracing this new technology:
    - Cellular meats being developed by companies in China, Australia and Brazil
    - Cell based salmon and human milk in the USA who echo arguments of safety as cellular foods are not at risk of being exposed to environmental pollutants
- Garwood (2023) of the Food Institute lists dairy products including such as cheese and yoghurt, and ice cream in addition to bakery products such as bread produced through precision fermentation

<u>Medicines and health</u>

In 1978 the first human insulin was genetically engineered harnessing the production machinery of the bacteria *E.coli.* Bioengineered yeast has been used to produce a precursor for artemisinin an anti-malaria drug as revealed by Ro *et al* (2006). Since then bioengineering has increasingly been used in medicine for diagnoses, treatments such as antibacterial patches and health monitoring including the accelerated development of vaccines. In addition to pharmaceutical drugs from genetically modified organisms (GMOs) are an increasing number of biomaterials used in medical applications some of which are outlined below. There are greater concerns over the future possible use of human gene editing rather than gene therapy. For example Vokinger, Glaus and Kesselheim (2023) report that “13 gene therapies have been approved in the US, 15 in the EU, and 9 in Switzerland” whereas genome-editing is generally banned by regulations, guidelines or laws.

Materials and chemicals

Some examples of directly bioengineered materials and monomer precursors for polymers that show promise in their own right or illustrate how the state of the technology has enabled tools to be applied to modify the products of cellular metabolism are listed here in no particular order:

- Beyer *et al* (2018) created a gel that could trap or release molecules dependent on exposure to light, which could even “count” light pulses.
- Luo *et al* (2017) developed a thermoresponsive elastin-b-collagen for targeted drug delivery.
- Le Feuvre and Scrutton (2018) are avid promoters of the potential for synthetic biology to develop materials for use in bioelectronics, biocomputing, biosensing and bioenergy, in addition to self-healing materials.
- Roberts *et al* (2019) give details on a range of synthetic biology developments of adhesives, fibres and camouflage materials, some with potential applications in the aerospace industry.
- A timeline of milestones in synthetic biology in the last decade, by Tang *et al* (2020), along with a table of applications, illustrates rapid developments in bioelectronics, fibre innovations such as the production

of silkworm and spider silks, amyloid underwater adhesives and deep learning tools for antibiotic discovery and several other smart material applications.

- Burgos-Morales *et al* (2021) make a good case for synthetic biology becoming a driving force behind the development of a number of multifunctional materials with “self-“ properties of -growth, -assembly, -adaptability, and -healing.

Renewable fuels

First and second generation biofuels tend to be based on the production of (bio)ethanol from starch based feedstocks using yeasts, the product is then blended to various extents with hydrocarbons from petroleum. There have been a number of studies looking at the possibility of using cellulose and / or lignin from crop residues for bioethanol fermentation. However, some of the disadvantages of using ethanol include miscibility with water, volatility, energy content. Butanol has advantages of higher energy content, lower volatility, and lower miscibility with water making a potential candidate for use in blended fuel. It can be fermented using *Clostridium acetobutylicum* which produces biobutanol amongst other products. To improve on the growth rate and using the more fully studied *E.coli* genome, Atsumi *et al* (2008) explored the deletion of some genes along with transfer and amplification of others. The results then showed some promise. A more recent review by Abdelaal *et al* (2022) indicates that further research needed to further develop production methods such as the light regulation of biobutanol production using *Saccharomyces cerevisiae* by Zhao *et al* (2018).

Although the UK may be intending to phase out carbon based transport vehicles there are a number of opportunities for UK research and industries to take a lead in the development of bioengineered fuels. This would potentially support ambitions to increase energy security.

Environmental applications including carbon cycling

The use of precision bioengineered fermentation in food production has been illustrated above. Researchers including Jahn, Rekdal and Sommer (2023) or Choi, Yu and Lee (2022) emphasise the low environmental footprint and ability to utilise a range of feedstocks help to champion the adoption of precision fermentation in the production of foods to feed ever growing populations. Waller (2024) adds to this how the use of these foods also takes pressure off land use for agriculture freeing up some land for conservation of biodiversity or other use environmentally beneficial purposes such as water capture, storage or aquifer recharge systems.

Teng *et al* (2021) discuss the potential for synthetic biological technology to upcycle food waste, such as surplus bread for malted barley used by the Singaporean CRUST company and use non-food substrates in precision fermentation.

Zrimec *et al* (2021) found, through bioprospecting, that the global microbiome has a very wide variety of enzymes showing potential for plastic degradation. If these could be harnessed for waste digestion there is a route for reducing or cleaning up plastic pollution.

Regarding fungi, the abstract from a white paper, one of the outcomes, of the 2nd Think Tank meeting held by the Berlin EUROFUNG consortium in 2019 puts it this way:

> Fungi have the ability to transform organic materials into a rich and diverse set of useful products and provide distinct opportunities for tackling the urgent challenges before all humans. Fungal biotechnology can advance the transition from our petroleum-based economy into a bio-based circular economy and has the ability to sustainably produce resilient sources of food, feed, chemicals, fuels, textiles, and materials for construction, automotive and transportation industries, for

furniture and beyond. Fungal biotechnology offers solutions for securing, stabilizing and enhancing the food supply for a growing human population, while simultaneously lowering greenhouse gas emissions. Fungal biotechnology has, thus, the potential to make a significant contribution to climate change mitigation and meeting the United Nation's sustainable development goals through the rational improvement of new and established fungal cell factories. (Meyer *et al*, 2020).

5. What are the risks posed to society by engineering biology?

According to Munsie and Gyngell (2018) in April 2015 a research group in China used genome editing on 'non-viable 'IVF human embryos to attempt correction of the β – thalassaemia gene. Since then a number of countries and international organisations (e.g. UNESCO) have called for a ban on embryo gene editing as did the US National Institutes of Health, although both the Hinxton Group and the International Society for Stem Cell Research guidelines do not go that far.

Key principles in bioethics include justice, autonomy, beneficence and non-maleficence. Although the intention of engineering biology is to improve the lives of people this does not mean that there will be unintentional harm done to the environment and other living entities through horizontal gene transfer (HGT) and disruption to food chains, webs or natural cycling systems. There are many people who view this type of harm as morally unacceptable due the intrinsic value of all living species, and others who see that this may well be imprudent due to potential loss of instrumental value of nature to sustainably provide the complete suite of ecosystem services. One may also ask whether engineering biology can be completely 100% confident that unintentional transfer of hidden viral genes passed into other organisms with unforeseen and formerly never encountered consequences. What measures are being taken to prevent or at least minimize this risk?

a. There are regulatory, ethical, and safety concerns that go along with any dual-use technology, particularly in the case of gene-editing. What are the major areas of concern?

The lack of international laws and regulations over the safe and ethical use of genetic engineering in medical procedures is a concern and there are worries that permitting such research could be the beginning of a slippery slope. The concerns are primarily related to non-therapeutic or gain of function research. Further bioethical considerations include:

- The inability to gain consent from embryos subjected to gene-editing or gene therapy;
- As there are some unknown risks, can truly *informed* consent ever be given?
- Is there inequity if this technology is only available to the wealthiest in society?
- Could this lead to a new class of people defined by their genetic enhancements?
- Recognising that all living organisms have intrinsic value in their own right, there is an ethical obligation for humans not to put other species at risk from the release of transgenic organisms into the environment where HGT could impact native species and even ecosystems as a whole.

Ou and Guo (2023) recommend biocontainment using “kill switches” and auxotrophic organisms amongst other tools to help minimize risks, as so many of these risks are nearly impossible to predict or quantify. In short current laws and regulations are insufficient and therefore it is incumbent upon researchers, their institutions and funding bodies to ensure that measures are in place to protect us all from any potential harm from malicious applications of synthetic biology.

b. i) Does engineering biology pose national security risks and if so, what are they?

Although the origin of the SARS-Cov-2 virus is not known there are some arguments that claim it to have been released from a laboratory possibly studying gain of function research. This is not beyond the realms of possibility as in 2012 a Dutch researcher did create an H5N1 virus, which raised fears of uses of bioengineering in bioterrorism. Branswell (2022) draws attention to the reported production of novel SARS-Cov-2 viral strains at Boston University which is unwise and could be disastrous if they ended up in the hands of bioterrorists.

In agriculture the main concern is from horizontal gene transfer, which could potentially pose a risk to the integrity and ultimately the health of natural ecosystems.

c. i) What early warning systems are in place, both nationally and internationally, to monitor whether engineering biology is being misused?

In the USA the United States Department of Agriculture (USDA) approves the overall use of genetically modified plants in the environment, the Food and Drug Administration (FDA) oversees crops intended for food, animal feed and pharmaceutical uses, whereas the Environmental Protection Agency (EPA) regulates the use of crops with disease and pesticide resistance, according to Byrne (2014). Whether this level of regulation before genetically modified crops are used in all other countries where they are grown is not certain.

The United Nations Food and Agriculture Organisation (2022b) states that we can: “be rest assured that GM crops are approved and safe and continuous monitoring is undertaken.” Whether this satisfies the UK public is yet to be determined.

Article 1 of the Universal Declaration of Bioethics and Human Rights (2005) states that it addresses ethical issues in the medical, life sciences and associated technologies. In Article 2 one of the aims is explicitly recognises the value of scientific research and technological developments, but emphasises that these must be conducted by adhering to ethical principles the declaration specifies. This declaration has been signed by many states across the world, but it is a soft law of guiding principles. That is not to say that it had no influence, but it does mean that if a state was to deliberately conduct gain of function research for the maleficent intent or purpose then the UDBHR would have little power to prevent them.

Many countries around the world have bioethics committees such as the Nuffield Council on Bioethics, yet bioethics in America tends to focus more on biomedical ethics and has little remit to deliver on environmental ethics or ethical considerations of living (biological) entities generally. This is a problem when considering synthetic biology as there are the potential risks of impacts beyond just the health and wellbeing of humans. UNESCO established the International Bioethics Committee in 1993 and various topics have been debated, providing cross-cultural approaches to bioethics and genetic manipulation.

There are some overall guidelines in the Convention on Biological Diversity (CBD) as this has regulations that relate to issues of justice including:

- conservation of biodiversity for generations in the future – which could be lost if too much emphasis is placed on growing bioengineered crops that enable HGT

- equitable and fair use of genetic resources – which could be in jeopardy if genes become "owned" by big corporations and if their GMOs are not affordable to less affluent people
- obtaining informed prior consent for the use of genetic resources – which could prove difficult to regulate if genetic material is obtained from certain ecosystems and other countries or from landraces that other people have put the hard work into developing

The International Society for Systems Biology, Synthetic Biology Leadership Council and the World Health Organisation are also, or already have developed some guidelines. However, as bioengineering possibilities are changing quickly there must be some adaptability and flexibility allowed for within any regulations for reasons of biosecurity and safety. If regulations are too rigid this may hamper further beneficial research and development.

ii) Are these sufficient, or is further regulation needed, for example setting out what DNA synthesis technology can be used for?

There is some provision for the development of new crops in the UK through the Genetic Technology (Precision Breeding) Act 2023. Yet this will limit gene transfer from other species as it defines precision bred organisms as those could have resulted from traditional breeding technologies. The examples listed in response to question 2 a clear illustration of many positive benefits for the use of GMOs in a changing world. Archibald, Zhong and Brophy (2023) urge policy makers, scientists and engaged public to work together to open up possibilities that are currently not allowed in the UK, China and countries such as Mexico that has banned the production of GM corn. Sun *et al* (2022) for example call for a combination of hard and soft law to regulate the research and use of synthetic biology in China. The EU the laws governing the use of GMOs are more than two decades old and according to Ramsay *et al* (2022) have not kept pace of developments in

DNA technology. For example the GMO Directive may hinder the development of precision breeding. Restrictions on the use of them should be dealt with within categories rather than a blanket ban. Similar concerns are expressed by Kendig *et al* (2024) of a lack of bioethics commissions during the last decade in America and that there is a need for debate and regulations regarding food and new agricultural biotechnology.

The Engineering Biology Research Consortium propose six ethical principles that would be a prudent to adhere to, as detailed by Mackelprang *et al* (2021):

- synthetic biology should be used for benefits to people, society and the environment;
- these benefits should outweigh harms;
- to ensure there is equity and justice at all stages of engineered biology from education all the way through research and development to commercialization;
- to share the benefits and knowledge of synthetic biology
- to protect people's rights – both freedom of inquiry and informed consent
- to promote open and transparent communication between all interested parties

7. What possible barriers and limitations to good and effective use of engineering biology?

b. i) What more can the Government do to foster public understanding of engineering biology?

A detailed report by the British Science Association (2023) found that:

- There is limited recent social science data on the UK public's understanding of engineering biology
- People's attitudes depend on their personal values and the context
- People have concerns regarding safety, unfair access to the benefits, and misuse
- Policy leaders perception that people are opposed to engineering biology may be based on former objections to genetically modified foods
- People with greater awareness are more likely to support engineering biology proposals to solve problems that are faced within society

A previous survey found there was an increase in awareness of this technology, but this does not imply a depth of understanding. It did however find that those who had a better understanding were more likely to be in support for it. However, Haga *et al* (2013) also found that as people gained understanding through a *Genome Dinner* series of pilot study activities they also were more accepting of genetic manipulation technology. Collectively these data imply that greater education of genetic biology will generally enable people to make choices, and that a greater proportion of people making informed choices tend towards accepting this new technology, whilst still expressing some reservations.

Many accessible resources have been developed by internationally well regarded institutions such as the FAO (2022b) *Genetically Modified Crops: Safety, benefits, risks and global status* or the UNDP *Learning for Nature* platform that offers free online courses. Schools and even adult education providers should be encouraged to offer courses to support students learn to become citizens equipped to thrive sustainably. Since science education is compulsory in the UK to a certain age, then it would be relatively straight forward to ensure that an in depth and balanced curriculum is developed to ensure students develop informed opinions for themselves regarding synthetic biology even though some will also be heavily influenced by their established personal values and religious beliefs.

Writing in Australia, Carter and Mankad (2021) identify one of the key actions to promote acceptance of synthetic biology is to value different people's philosophical perspectives. Tallapragada *et al* (2020) demonstrate how the majority of people respond better to concrete rather than abstract examples when making decisions in favour of GM technology.

When discussing acceptance of robotics and artificial intelligence, Winfield and Jirotka (2018) clearly show how ethical governance is a must. The same will apply to public acceptance of bioengineered products and GMOs generally. This governance clearly needs to be transparent, equitable, just and based on scientific data.

ii) Is public acceptability of these technologies a barrier to deployment in the UK?

Part of the problem regarding the acceptance of new technologies is that the general public do not necessarily approach considerations of risk in the same way as scientists. It is not merely a case of understanding how the technology works. Regarding the lack of acceptance of GM crops in the UK twenty years ago Burke (2004) wrote:

> "… the public's reaction to risk is often rather different to that of scientists, and can occur as outrage (the way the public regards Monsanto), dread (as many would regard a nuclear power station explosion) and stigma (the way the public regards food irradiation)."

This is where the greatest barrier to public acceptance of synthetic biology may lie as scientists, policy makers and the general public may approach synthetic biology from very different perspectives and make different conclusions regarding its use and safety. Therefore any education programme needs to address these preconceptions and fears respectfully.

Given that our experience over the past few decades has seen divisions between technophiles and technophobes, and very legitimate differences in the perception of risk between people, not every citizen will approve any specific application. Better education in dialogue skills and social harmony will be important to develop concurrent with specific ethical and social analysis of any technology, so that even if no consensus is possible, there is respect for the informed choices of citizens that opt in to use novel technologies. At the same time, dialogue about the reasons why some people oppose modification of nature, as we embrace a future vision of our world.

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References

Abdelaal, A.S. and Yazdani, S.S. (2022) “Engineering of *E. coli* to synthesize butanol” *Biochem Soc Trans* 50(2): 867-876 doi:10.1042/BST20211009.

Archibald, B.N., Zhong, V. and Brophy, J.A.N. (2023) “Policy makers, genetic engineers, and an engaged public can work together to create climate-resilient plants. *PLoS Biol* 21(7): e3002208. [Accessed online 27-4-24. Available from: https://doi.org/10.1371/journal.pbio.3002208].

Atsumi, S., Cann, A.F., Connor, M.R. *et al.* (2008) “Metabolic engineering of *Escherichia coli* for 1-biobutanol production” *Metabolic Engineering* 10: 305-311 doi:10.1016/j.ymben.2007.08.003

Aziz, M.A., Brini, F., Rouached, H. and Masmoudi, K. (2022) “Genetically engineered crops for sustainably enhanced food production systems” *Frontiers in Plant Science* 13:1027828 doi: 10.3389/fpis.2022.1027828

Beyer, H.M., Engesser, R., Hörner, M., Koschmieder, J., Beyer, P., Timmer, J., Zurbriggen, M.D. & Weber, W. (2018) “Synthetic Biology Makes Polymer Materials Count” *Adv Mater.* 30(21):e1800472. doi: 10.1002/adma.201800472.

Branswell, H. (2022) “Boston University researchers ’testing of lab-made version of Covid virus draws government scrutiny” StatNews [Accessed online 3-5-24. Available from: https://www.statnews.com/2022/10/17/boston-university-researchers-testing-of-lab-made-version-of-covid-virus-draws-government-scrutiny/].

British Science Association (2023) *Public perceptions of engineering biology Part 1: Health applications* [Accessed online 27-4-24. Available from: https://sciencewise.org.uk/2024/01/public-perceptions-of-engineering-biology-health/].

Burgos-Morales, O., Gueye, M., Lacombe, L., Nowak, C., Schmachtenberg, R., Hörner, M., Jerez-Longres, C., Mohsenin, H., Wagner, H.J. and Weber, W. (2021) “Synthetic biology as driver for the biologization of materials sciences” *Materials Today Bio* 11: 100115 [Accessed online 3-5-24. Available from: https://doi.org/10.1016/j.mtbio.2021.100115].

Burke, D. (2004) “GM food and crops: what went wrong in the UK? Many of the public's concerns have little to do with science” *EMBO Rep.* 5(5):432-6. doi: 10.1038/sj.embor.7400160.

Byrne, P. (2014) *Genetically Modified (GM) Crops: Techniques and Applications.* Fact Sheet 0.710 Crop Series: Production, Colorado State University [Accessed online 25-4-24. Available from: https://extension.colostate.edu/topic-areas/agriculture/genetically-modified-gm-crops-techniques-and-applications-0-710/].

Carter, L., and Mankad, A. (2021) “The Promises and Realities of Integration in Synthetic Biology: A View From Social Science” *Front Bioeng Biotechnol*. 8:622221. doi: 10.3389/fbioe.2020.622221.

Choi, K.R., Yu, H.E., Lee, S.Y. (2022) “Microbial food: microorganisms repurposed for our food” *Microbiology and Biotechnology* 15(1):18-25. doi:10.1111/1751-7915.13911

FAO (2022a) *Cell-based food: its safety and its future role*. Food and Agriculture Organization of the United Nations, Rome. [Accessed online 17-4-24. Available from: https://www.fao.org/documents/card/en/c/cc6967en].

FAO (2022b) *Genetically modified crops: Safety, benefits, risks and global status* FAO, Colombo, Sri Lanka [Accessed online 28-4-24. Available from: https://openknowledge.fao.org/items/8f6dbea3-503a-4072-9712-010c4b61b816].

Garwood, G. (2023) *What's Next in Precision Fermentation?* The Food Institute. [Accessed online 16-4-24. Available from: https://foodinstitute.com/focus/whats-next-in-precision-fermentation/].

Haga, S.B., Rosanbalm, K.D., Boles, L., Tindall, G.M., Livingston, T.M. & O'Daniel, J.M. (2013) “Promoting public awareness and engagement in genome sciences” *J Genet Couns*. 22(4):508-16. doi: 10.1007/s10897-013-9577-3.

Hilgendorf, K., Wang, Y., Miller, M.J., Jin, Y.S. (2024) “Precision fermentation for improving the quality, flavor, safety, and sustainability of foods” *Current Opinions in Biotechnology* 86:103084 doi:10.1016/j.copbio.2024.103084.

Jahn, L.J., Rekdal, V.M., Sommer, M.O.A. (2023) “Microbial foods for improving human and planetary health” *Cell*. 186(3):469-478. doi:10.1016/j.cell.2022.12.002.

Kendig, C., Selfa, T., Thompson, P. B., Anthony, R., Bauchspies, W., Blue, G., *et al* (2024) "The need for more inclusive deliberation on ethics and governance in agricultural and food biotechnology" *Journal of Responsible Innovation*, 11(1). [Accessed online 28-4-24. Available from: https://doi.org/10.1080/23299460.2024.2304383].

Khokhar A., Shahbaz, M., Maqsood, M.F., Zulfiqar, U., Naz, N., Iqbal, U.Z., Sara, M., Aqeel, M., Khalid, N., Noman, A., Zulfiqar, F., Al Syaad, K.M., and AlShaqhaa, M.A. (2023) "Genetic modification strategies for enhancing plant resilience to abiotic stresses in the context of climate change" *Funct Integr Genomics* 23(3):283. doi: 10.1007/s10142-023-01202-0.

Le Feuvre, R.A. & Scrutton, N.S. (2018) "A living foundry for Synthetic Biological Materials: A synthetic biology roadmap to new advanced materials" *Synth Syst Biotechnol*. 3(2):105-112. doi: 10.1016/j.synbio.2018.04.002.

Luo, T., David, M.A., Dunshee, L.C., Scott, R.A., Urello, M.A., Price, C., and Kiick, K.L. (2017) "Thermoresponsive Elastin-b-Collagen-Like Peptide Bioconjugate Nanovesicles for Targeted Drug Delivery to Collagen-Containing Matrices" *Biomacromolecules* 18(8):2539-2551. doi: 10.1021/acs.biomac.7b00686.

Mackelprang, R. *et al* (2021) "Guiding Ethical Principles in Engineering Biology Research" *ACS Synthetic Biology* doi: 10.1021/acssynbio.1c00129.

Meyer, V., Basenko, E.Y., Benz, J.P., Braus, G.H., Caddick, M.X., Csukai, M., de Vries, R.P., Endy, D., Frisvad, J.C., Gunde-Cimerman, N., Haarmann, T., Hadar, Y., Hansen, K., Johnson, R.I., Keller, N.P., Kraševec, N., Mortensen, U.H., Perez, R., Ram, A.F.J., Record, E., Ross, P., Shapaval, V., Steiniger, C., van den Brink, H., van Munster, J., Yarden, O., Wösten, H.A.B. (2020) "Growing a circular economy with fungal biotechnology: a white paper" *Fungal Biol Biotechnol* 7:5. doi: 10.1186/s40694-020-00095-z.

Munsie, M. and Gyngell, C. (2018) "Ethical issues in genetic modification and why application matters" *Curr Opin Genet Dev.* 52:7-12. doi: 10.1016/j.gde.2018.05.002.

Ou, Y. and Guo, S. (2023) "Safety risks and ethical governance of biomedical applications of synthetic biology" *Front. Bioeng. Biotechnol.* 11:1292029. doi: 10.3389/fbioe.2023.1292029

Ramsay, T., Robinson, B., Coche, I., Hackett, K. and Emerson, C. (2022) “Ethical aspects of GMO regulation in the EU” *EMBO Reports* 23(9):e55583. doi: 10.15252/embr.202255583 [Accessed online 27-4-24. Available from: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC9442288/pdf/EMBR-23-e55583.pdf].

Ro, D.K., Paradise, E., Ouellet, M. *et al*. (2006) “Production of the antimalarial drug precursor artemisinic acid in engineered yeast” *Nature* 440: 940–943 https://doi.org/10.1038/nature04640.

Roberts, A.D., Finnigan, W., Wolde-Michael, E., Kelly, P., Blaker, J.J., Hay, S., Breitling, R., Takano, E. and Scrutton, N.S. (2019) “Synthetic biology for fibres, adhesives and active camouflage materials in protection and aerospace” *MRS Communications* 9(2):486-504 doi: 10.1557/mrc.2019.35.

Sharma, P., Singh, S.P., Iqbal, H.M.N., Parra-Saldivar, R., Varjani, S. and Tong, Y.W. (2022) “Genetic modifications associated with sustainability aspects for sustainable developments” *Bioengineered* 13(4):9508-9520. doi: 10.1080/21655979.2022.2061146.

Sun, T., Song, J., Wang, M., Zhao, C. and Zhang, W. (2022)” Challenges and recent progress in the governance of biosecurity risks in the era of synthetic biology” Journal of Biosafety and Biosecurity 4(1): 59-67 [Accessed online 27-4-24. Available from: https://doi.org/10.1016/j.jobb.2022.02.002].

Tallapragada, M., Hardy, B.W., Lybrand, E. and Hallman, W. (2020) “Impact of Abstract Versus Concrete Conceptualization of Genetic Modification (GM) Technology on Public Perceptions” *Risk Analysis* 41(3) doi: 10.1111/risa.13591.

Tang, T.C., An, B., Huang, Y. *et al.* (2021) “Materials design by synthetic biology” *Nat Rev Mater* 6: 332–350 [Accessed online 1-5-24. Available from: https://doi.org/10.1038/s41578-020-00265-w].

Teng, T. S., Chin, Y.L., Chai, K.F. and Chen, W.N. (2021) “Fermentation for future food systems” *EMO reports* 22:e52680 [Accessed online 14-4-24. Available from: https://www.embopress.org/doi/epdf/10.15252/embr.202152680].

Vokinger, K.N., Glaus, C.E.G. & Kesselheim, A.S. (2023) “Approval and therapeutic value of gene therapies in the US and Europe” *Gene Therapy* 30:

756–760 [Accessed online 6-5-24. Available from: https://doi.org/10.1038/s41434-023-00402-4].

Waller, A.R. (2024) *page 5 of written evidence for the Climate Change and Security Inquiry submitted online 26-4-24; currently under consideration by the Environmental Audit Committee.*

Winfield, A. F. T. and Jirotka, M. (2018) "Ethical governance is essential to building trust in robotics and artificial intelligence systems" Phil. *Trans. R. Soc.* A.37620180085 [Accessed online 27-4-24. Available from: http://doi.org/10.1098/rsta.2018.0085].

Zhao, H., Wang, Q., Liu, C., Shang, Y., Wen, F., Wang, F., Liu, W., Xiao, W., and Li, W. (2018) "A Role for the Respiratory Chain in Regulating Meiosis Initiation in *Saccharomyces cerevisiae*" *Genetics* 208(3):1181-1194 [Accessed online 5-5-24. Available from: https://academic.oup.com/genetics/article/208/3/1181/6066480].

Zrimec, J., Fu, X., Muhammad, A.S. *et al*. (2022) "Controlling gene expression with deep generative design of regulatory DNA" *Nat Commun* 13: 5099 [Accessed online 27-4-24. Available from: https://doi.org/10.1038/s41467-022-32818-8].