Dear All,

I want to first thank Mr. Linnestad for moderating such a robust discussion so far. My name is Todd Kuiken and I am a Senior Research Scholar with the Genetic Engineering & Society Center at North Carolina State University. Prior to joining NC State I led the Synthetic Biology Project at the Woodrow Wilson International Center for Scholars. I have had the privilege to serve on the AHTEG on synthetic biology. Since I am joining the discussion towards the end and many issues have been raised and debated already, I would like to focus my intervention around technology trends, along with data and funding gaps as they relate to the guiding questions posed to the forum.

Without minimizing the potential positive/negative impacts prior synthetic biology applications pose; the technology trend seems to be moving from “relatively” simple organisms (i.e. e-coli and yeast) to more complex organisms and environmental systems. Jim Thomas [#8437] provided a useful list and I would like to expand upon this using U.S. DARPA programs to illustrate this trend. Let me state clearly that I am not qualifying these DARPA programs as positive or negative. These programs provide examples of where the synthetic biology field may be moving towards and provide a window towards future applications that could have a direct impact on the objectives of the convention. While the phrase “synthetic biology” does not show up in DARPA budget documents until 2011, funding for “synthetic fuels,” “synthetic cells,” and “synthetic chromophores” begin to appear in 2008 and continued through 2010. Since then, DARPA has developed five programs, listed here in chronological order, that demonstrate the growing complexity of synthetic biology under development that could have a direct impact on the objectives of the convention.

The first program, called “Living Foundries”, launched in 2013. This program: “seeks to transform biology into an engineering practice by developing the tools, technologies, methodologies, and infrastructure to increase the speed of the biological design-build-test-learn cycle while significantly decreasing the cost and expanding the complexity of systems that can be engineered. The technologies and infrastructure developed as part of this program are expected to enable the rapid and scalable development of transformative products and systems that are currently inaccessible. Examples include novel materials, industrial chemicals, pharmaceuticals, and improved agricultural products (DARPA 2016a, Living Foundries Program).

The second program, called “Biological Robustness in Complex Settings” (BRICS), launched in August 2014. This program “seeks to develop the fundamental understanding and component technologies needed to engineer bio-systems that function reliably in changing environments. A long-term goal is to enable the safe transition of synthetic biological systems from well-defined laboratory environments into more complex settings where they can achieve greater biomedical, industrial, and strategic potential” (DARPA 2016b, BRICS).

The third program, “Safe Genes,” was announced in September 2016 and includes gene drives. This program is meant to “create biological capabilities that enable the safe pursuit of advanced genome editing applications.” According to the website: “Implementation of a ‘safety first’ approach to the development of next generation biotechnologies and genome editing tools and their derivative technologies (e.g., gene drives) will foster, and even accelerate, responsible innovation while mitigating the risk of unintended consequences. The Safe Genes program will provide new insights into what is possible, probable, and vulnerable with regard to genome editing biotechnologies and their derivative applications, create novel tools to enable predictable and reversible control of gene editors, and counter unwanted genome editing activity and outcomes” (DARPA 2016c, Safe Genes Proposers Day).

The fourth program, Insect Allies, was announced in November 2016. This program: “Aims to transform certain insect pests into ‘Insect Allies,’ by modifying insects to disseminate targeted genetic payloads to plant populations in order to protect crops from potential plant pathogens that are either naturally occurring or are intentionally designed and released to cause harm” (DARPA 2016d, Insect Allies). Finally, the fifth DARPA program, entitled “Ecological niche-preference engineering,” announced in 2017 centers around “the development of technologies that enable the genetic engineering of an organism's preference for a niche (e.g., temperature range, food source, and habitat). DARPA envisions creating genetic engineering strategies to control and alter the niche preferences of organisms to reduce economic, health, and resource burdens. A fundamental component of this work will be to expand our understanding of the genetic, epigenetic, and molecular contributors to the establishment of niche preference” (DARPA 2016e, Ecological Niche Preference).

Gene drives provide a good example of the gaps in knowledge that exist when attempting to address the guiding questions posed in this forum. The scientific data surrounding the feasibility and ecological implications of gene drives is limited. Besides a few laboratory studies most of the scientific literature ascribing the benefits and risks of gene drives have been based on models and are not comprehensive to address the broad scope of the questions posed in this forum [ (Hammond, et al. 2016) (Gantz, Jasinskiene, et al. 2015) (Gantz and Bier, The mutagenic chain reaction: A method for converting heterozygous to homozygous mutations 2015) (Di Carlo, et al. 2015) (Eckoff, et al. 2016) (Beaghton, Beaghton and Burth 2016) (Unckless, Clark and Messer 2017) (Reed 2017) (Esvelt, et al. 2014) (Noble, Olejarz, et al. 2017) (Noble, Min, et al. 2016) (Drury, et al. 2017) ].

As referenced by the U.S. State Department [#8550] the report produced by the Woodrow Wilson International Center for Scholars prioritized key research areas for government agencies, academia and industry to fund (Drinkwater, et al. 2014). Research areas include species for comparative research; phenotypic characterization; fitness, genome stability and lateral gene transfer; control of organismal traits; monitoring and surveillance; modeling and standardization of methods and data. The report says it is necessary to establish and sustain interdisciplinary research groups in order to conduct the research. Long-term support is also needed to address complex questions about how synthetic biology could affect the environment and overcome communication barriers across disciplines. However, there is still a significant funding gap that will need to be addressed in order to evaluate synthetic biology applications moving forward. An analysis of the U.S. federal research budget for synthetic biology suggests there is insignificant efforts to examine the ecological implications of these types of applications (Kuiken, U.S. Trends in Synthetic Biology Research Funding 2015). Subsequently the U.S. National Academies report on gene drives concluded that there is insufficient evidence available at this time to support the release of gene-drive modified organisms into the environment (National Academies of Sciences 2016).

The Genetic Biocontrol of Invasive Rodents program is one example that may provide additional information for this effort. In full disclosure, I am a part of this program and therefor will not ascribe its potential benefits or risks, but simply as an example of a comprehensive program that is attempting to address the overarching questions posed to this forum in relation to synthetic biology and could have a direct impact on the objectives of the convention. The program is still in its early stages and there is limited data. For an independent overview of the program, please visit: <http://www.audubon.org/magazine/summer-2017/how-genetically-modified-mice-could-one-day-save>

Finally, there were many interventions during this opening discussion around access and benefits sharing issues. It is my understanding that there is an online forum and AHTEG being formed under the Nagoya Protocol to examine these issues, specifically in regards to digital sequence information. It may be helpful for the moderator to specify which topic areas will be addressed there.

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