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Comments to the EPA workshop on regulation of synbio algae

Good Morning

I am Jaydee Hanson, Policy Director for Emerging Technologies (including synthetic biology) at the International Center for Technology Assessment. We are happy that EPA is revising its regulations for the oversight of synbio organisms. In 2010, we called for the agencies of the US government to quit pretending that the coordinated framework was adequate for regulating synthetic biology and issued with some 120 other groups, the Principles for the Oversight of Synthetic Biology. These comments support the Principles before recommending improvements to TSCA for synbio organisms.

EPA uses the Toxic Substance Control Act to regulate microorganisms. TSCA is inadequate for microorganisms intended to produce specific chemicals in enclosed containers and it is more inadequate for the regulation of synbio algae grown in ponds with still greater environmental interactions. Moreover, EPA's staffing is inadequate for the flood of new synbio organisms. Some companies with large synthetic biology programs, including those producing algal biofuels, may consider dozens or even hundreds of variants of their microbial products during product development, each of which would require an EPA review of a TSCA Environmental Release Application (TERA) for field testing.

EPA cannot process the deluge of new applications with the same thoroughness that it used to review TERAs and Microbial Commercial Activity Notices (MCAN) to date. Synbio organisms will come from a broader diversity of microbes than the dozen organisms widely used today. As such, the EPA will need to develop greater and more specialized expertise, requiring training existing staff or making new hires. If EPA's TSCA Biotechnology Program does not receive more resources to keep pace with the anticipated workload, longer review times may become more common or inadequate reviews will occur, increasing the likelihood that the agency will be sued. Whether from slow reviews or reviews stopped because the EPA faces legal challenges, product developers will be frustrated.

EPA officials may be tempted to review and approve MCANs and TERAs on a programmatic level where multiple, related notifications or applications can be processed together, but this may raise additional questions about whether such programmatic reviews address the concerns of groups like mine that each synbio organisms be reviewed specifically, not just as a class.

While the agency's experience in regulating microbes has been limited, EPA officials have argued that the agency has reasonably strong pre-market authorities to ask for data and information from product developers, both during the TERA process and when product developers move toward commercialization of their products

by submitting MCANs. EPA officials have argued that the agency has adequate authority to impose conditions on manufacture or use of engineered microbes to ensure their safe use through the use of Consent Orders and “Significant New Use Rules.” The agency recently proposed a Significant New Use Rule relating to a genetically engineered strain of *Trichoderma reesei* used in the production of enzymes for ethanol. EPA officials were concerned that under some conditions of use, the microbe would not be contained to the appropriate level and might generate peptides with toxic characteristics; the proposed SNUR would allow EPA to evaluate a new intended use of the microbe and prohibit or limit that use if it may be hazardous. This SNUR demonstrates an important tool that EPA has available, but the White House Office of Management and Budget has tried to limit how the EPA uses SNURs for nano-chemicals and it will likely limit their use for synthetic biology. This is not the appropriate response.

Regardless, EPA’s experience using TSCA for engineered microbes is limited, and questions have been raised whether TSCA gives EPA officials sufficient authority to require necessary, but expensive tests to place conditions on use, or to prevent the commercialization of a dangerous product. While product developers may agree to Consent Orders, they are not a legal requirement. TSCA requires that once a manufacturer submits an MCAN, notifying EPA that it intends to commercially produce a new intergeneric microbe, EPA officials then have 90 days to make a finding. If EPA would like to request more data or information, it must find that there is insufficient information to evaluate the human health and environmental effects of the substance, and either (1) that the microbe may present an unreasonable risk of injury to human health or the environment, or (2) that the microbe will be produced in substantial quantities and may be anticipated to enter the environment in substantial quantities or that there may be significant or substantial human exposure. This standard puts a substantial burden of proof on the agency and may be particularly difficult for the agency to meet when it is faced with increasingly novel microbes. In the absence of this finding, a product can move to market after the 90-day evaluation period even without the additional data. This timeline is only 60 days for the TERA.

For both the TERA and the MCAN, the short time-frame allowed to EPA officials to make a determination raises questions about the quality of review. In general, when product developers have been unable to comply with those requests, they have withdrawn the application or notification. As more and more applications come to EPA product developers may not be so cooperative. This process has not been challenged in court, so there is still much legal uncertainty.

Congress is currently considering several additional measures to strengthen EPA’s authority in TSCA. None of the bills being considered have specific language related to microorganisms, but the following ideas would help EPA with synbio organisms:

STRONG BURDEN OF PROOF MUST BE REQUIRED OF THE DEVELOPER ON SAFETY

- requiring product developers to demonstrate that there are no unreasonable adverse effects before a product can go to market; this will save the EPA time and money and make the entire process faster. It reduces the burden of proof required for EPA to pursue post-market restrictions. Such provisions could be developed specifically for intergeneric microbes under TSCA. This type of Congressional action would increase the authority

that EPA brings to bear in regulating intergeneric microbes, thereby improving the ability of EPA officials to minimize risks.

LONGER ASSESSMENT TIMES FOR EPA

- extending the assessment periods for environmental release applications and for pre-market notifications to allow a more thorough assessment by EPA;

POST MARKET REPORTING

- instituting mandatory post-market reporting requirements;

TRANSPARENCY

- prohibit claims of Confidential Business Information for data related to human health and safety and environmental effects; EPA should not allow companies to claim the name of their product or company as CBI.
- post all MCAN, TERA, SNURs for public review promptly. The public has a chance to comment on organisms being added to the Tier 1 and Tier 2 lists. The public should be afforded a chance to comment on new organisms being considered by the EPA and also on new uses of existing organisms previously reviewed by the EPA.
- microbes used for non-commercial purposes or which fall under other statutes must be added to EPA review or there may be some environmental releases of a genetically engineered microbe that do not have a commercial purpose and would therefore not be covered under TSCA and EPA's regulations. If there is no agency with jurisdiction over the release, even legitimate research in the open environment has no way of being reviewed and might legally happen without review.

DEFINITION OF INTERGENERIC MUST INCLUDE ALL NEW KINDS OF GENETIC ENGINEERING

- the definition of "intergeneric" needs to be expanded to include all forms of new synbio organisms, engineered using any DNA/RNA transfer techniques, so EPA's authority is clear.

SYNBIO ORGANISMS MUST BE TREATED AS NEW ORGANISMS

- Synbio engineered microorganisms could pose challenges to the safety of the dozen microbes to which the EPA has given Tier 1 and Tier 2 exclusions. EPA should require all synbio organisms to go through MCAN and TERA reviews even if they are using Tier 1 and Tier 2 organisms as their "platform" to develop a new organism. Even some of the simplest synbio organisms inserted into Tier 1 or Tier 2 organisms have been metabolically engineered with changes in 10 or more locations within the "platform" organism. This extensive re-engineering should require new review, not categorical exclusion by EPA.