INSTITUTE FOR AGRICULTURE AND TRADE POLICY

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National Science and Technology Council
Emerging Technologies Interagency Policy Coordination Committee
Office of Science and Technology Policy
Executive Office of the President
Eisenhower Executive Office Building
1650 Pennsylvania Ave.
Washington, DC 20504

Submitted electronically

RE: Docket No. FDA–2015–N–3403

Request for Information: *Clarifying Current Roles and Responsibilities Described in the Coordinated Framework for the Regulation of Biotechnology and Developing a Long-Term Strategy for the Regulation of the Products of Biotechnology*[1]

The Institute for Agriculture and Trade Policy (IATP)[2] appreciates this opportunity to respond to the Request for Information (RFI) concerning the revision of the Coordinated Framework (CF). IATP will respond to questions 3 and 5, posed in the RFI.

3. How can Federal agencies improve their communication to consumers, industry and other stakeholders regarding the authorities, practices and bases used to ensure the safety of the products of biotechnology?

Before Federal agencies devote more resources to focus groups, workshops and polling to improve communication about the agencies "authorities, practices and bases," the agencies should scrutinize what is being communicated, rather than merely the "how" of communication.

Currently, Federal agencies do not ensure the safety of the products of biotechnology under the guidance provided by the CF. For example, the Food and Drug Administration (FDA) does not vouch for the safety of the products of biotechnology. Rather, the agency informs the commercial applicant that it has reviewed such data and summaries of applicant studies as the applicant voluntarily submits. Then it writes to the applicant, for example:

> Based on the safety and nutritional assessment you have conducted, it is our understanding that Monsanto has concluded that corn products derived from this new variety are not materially different in composition, safety, and other relevant parameters from corn currently on the market, and that the genetically modified corn does not raise issues that would require premarket review or approval by FDA.…[A]s you are aware, it is Monsanto's responsibility to ensure that foods marketed by the firm are safe, wholesome and in compliance with all applicable legal and regulatory requirements (FDA Letter, 1996).[3]

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The product, or more precisely, the transgenic "event," is then deregulated without any post-approval monitoring of how the "event" performs when it or a similar "event" is reproduced as a transgenic seed. FDA and other U.S. agencies delegate to the applicants the responsibility for ensuring the safety of products derived from biotechnology.

However, applicant claims about the safety of their products[4] are not based on science, at least not on peer-reviewed science that is validated in post-market safety assessments of products of biotechnology. For example, in 2002, the National Research Council concluded that

> [C]laims concerning the lack of effects from the tens of millions of hectares of transgenic crops that have been planted in the United States during the last three years are nonscientific. There has been no environmental monitoring of these transgenic crops, so any effects that might have occurred could not have been detected.[5]

The regulatory decision to not monitor transgenic crops is likewise not the result of a positive determination of the safety of transgenic crops by Federal scientists on the basis of review of mandatory submissions of applicant data and information as specified by the relevant agencies.

Under the CF, agency deregulation of the products derived from the transgenic "event" on the basis of voluntary submissions of applicant data, usually subject to the commercialization applicant's Confidential Business Information (CBI) claims and therefore not available for peer-reviewed science, has not enabled Federal agencies to ensure the safety of products of biotechnology. Improving communication techniques and strategy about how Federal agencies deregulate transgenic events and products of biotechnology under the CF is unlikely to enhance public confidence in the scientific robustness of the commercialization approvals.

Federal agencies are exceedingly skilled at controlling media messages about regulatory failure and in restricting public access to regulatory scientists in the event of public and environmental health controversies.[6] However, controlling the message about the deregulation of the products of biotechnology is unlikely to improve public confidence in the regulatory system, but not because of the occasional failure to stay "on message."

Rather, the increasing and unsustainable disparity between diminished federal regulatory resources and commercial applicant demands for ever faster deregulation of more and more complex biotechnology events and products requires robust peer review of biotechnology product applicant science beyond what can be provided by regulatory scientists, no matter how competent individually. Federal agencies are understaffed and underfunded to perform scientifically robust risk assessments of the huge increase in commercialization applications for food and agricultural products derived from post-transgenic techniques.[7]

The relatively simple modifications of transgenic engineering are being supplanted by the techniques of synthetic biology. According to one research team,

> Synthetic biology and other new genetic engineering techniques will likely lead to an increase in the number of genetically engineered plants that will not be subject to review by USDA [U.S. Department of Agriculture], potentially resulting in the cultivation of genetically engineered plants for field trials and commercial production without prior regulatory review for possible environmental or safety concerns.[8]

Deregulating a product of plant synthetic biology because the transgenic event does not contain a USDA recognized pest, already a low standard for non-regulated status, has great potential to result in the Horizontal Gene Transfer (HGT) of DNA and/or RNA sequences not found in nature. The reason for the likelihood of HGT resulting from post-transgenic DNA and/or RNA sequences is the lack of reliability of current biological containment techniques. Three scientific committees reported to the European Commission in early 2015 that

> Currently available safety locks used in genetic engineering such as genetic safeguards (e.g. auxotrophy and kill switches) are not yet sufficiently reliable for SynBio. Notably, SynBio approaches that provide additional safety levels, such as the genetic firewalls, may improve containment compared with classical genetic engineering. However, no single technology solves all biosafety risks and many new approaches will be necessary.[9]

Furthermore, as one biosafety research team noted, "the higher the complexity of a biosafety device, the more prone it may be to disturbance and failure" because of multiple physiological burdens placed on the microbial host by the multi-device safeguard.[10] The same researchers state that building a genetic firewall against HGT from combinations of DNA or RNA not found anywhere in nature "could lead to an effective semantic containment within decades; however, this would not stop a refactored microbe from competing at the physiological level with natural flora and fauna during environmental release."[11] It is not known whether the HGT of a synthetically modified organism will survive in nature and outcompete wild and agricultural plants.

Unfortunately, given the current legislative paralysis in Congress, it is very unlikely that Federal agencies will receive authorities that are adequate to enable those agencies to ensure the safety of products of synthetic biotechnology. The relentless Congressional assaults on the budgets and mandates of agencies charged by statute with protecting public and environmental health, including pertaining to products of biotechnology, all but preclude agreement on such legislation in the foreseeable future.[12]

Therefore, it appears that what the revised CF will coordinate are regulations and policy under current authorities. A prime candidate for use of current authority is that given by the Plant Protection Act to the Animal and Plant Health Inspection Service to regulate "noxious weeds." APHIS has inexplicably declined to use this authority.[13]

The huge economic, environmental and public health costs of the 60 million plus acres of U.S. farmland (as of 2013) infested by 'super-weeds' resistant to multiple applications of the companion pesticides and herbicides of transgenic seeds[14] may not be repeated by the HGT of synthetically modified organisms to agricultural plants. Biosafety researchers believe that the potential for HGT can be limited to some extent by genomic design: "natural laws of genetic variation . . . should be respected in the *in vitro* construction of genomic segments. With regard to the formation of recombinant DNA molecules, this precautionary principle can validly contribute to the biosafety of the envisaged product of biosynthesis."[15] However, not all plant synthetic biologists will be inclined to observe this precautionary principle. Even then the interaction of the synthesized DNA with natural DNA sequences in plants may prove to be unpredictable. Out of an abundance of caution, the revised CF should require APHIS to use its "noxious weed" authority not only to regulate the present generation of "super-weeds," but also future generations of invasive species that may result from HGT of plant synthetic biology varieties.

5. Are there specific issues that should be addressed in the update of the CF or in the long-term strategy in order to increase the transparency, coordination, predictability and efficiency of the regulatory system for the products of biotechnology?

In 2004, a National Academy of Sciences report recommended various measures to make data and information submitted to Federal agencies concerning genetically engineered foods publicly accessible for peer review, for example, to "[c]ollect and make publicly available key compositional information on essential nutrients, known toxicants, anti-nutrients, and allergens of commonly consumed varieties of food" and to '[r]emove compositional information on GE foods from proprietary domains to improve public accessibility."[16] However, under CF, Federal agencies routinely grant Confidential Business Information (CBI) status to large portions of commercial applicant data and information submissions for products of biotechnology. As of 2007, "more than 5,000 granted U.S. patents currently cover ordinary DNA sequences," about a seventh of patents granted for DNA sequences in Europe, partly due to lower U.S. standards for what is non-obvious. Hence, the submission data of U.S. biotechnology applicants are already very well and broadly protected by U.S. patent law prior to the granting of CBI status.[17]

The routine granting of CBI claims impedes the robust peer-reviewed science that should be determinative of Federal science-based decision-making. According to one biosafety researcher, CBIclaims oftentimes marginally serve their legitimate purpose to protect commercial interests and unnecessarily limit transparency and public peer review of data submitted to regulatory authorities. CBI and proprietary claims also restrict access to transgene sequence data, transgenic seeds, and other GMO materials, which precludes the development of independent research and monitoring strategies. In the long run, such claims are counterproductive to the safe and responsible commercial development of GM technology as they hinder the accumulation of biosafety data in the open, peer-reviewed literature, which is needed for both public and scientific consensus-building on safety issues and for improvements to the risk-assessment procedure itself.[18]

In order to modernize the regulatory system for products of biotechnology, per the requirements of the July 2 White House memo that authorized this RFI[19], the breadth of CBI claims granted by Federal regulators of products of biotechnology should be restricted only to trade secrets, which are not protected by patents and copyrights, e.g., those pertaining to genomic sequencing software. Furthermore, Federal agencies should specify CBI criteria to ensure that applicant data and information pertaining to human, animal, plant and environmental health be made available for public and peer review, even in the event that applicants claim disclosure of such data would expose a trade secret. Applicant data and information can be made semi-anonymous, just as it is in financial regulatory reporting, e.g., by coding just the last four numbers of a credit card.

Under the present practice of indiscriminate granting of CBI claims, Federal regulators are deprived of the peer review of modern biotechnology data that is the bedrock of scientific consensus and method. Let us imagine that classical genetic engineering were to remain at a scientific standstill and applicant submissions were merely technological applications of the current state of genomic and genetic manipulation knowledge. Even so, data and information about products derived from classical genetic engineering still would merit robust peer review, rather than the well-known limitations of a confidential dialogue between the industry applicant and the relevant Federal regulator.

However, classical genetic engineering, while still producing transgenic applications presented to regulators for commercial approval, is being eclipsed by post-transgenic techniques that are patented under very broad claims. As transnational corporations acquire the patent portfolios of non-profit and for-profit start-up synthetic biology companies, open source arrangements for exchange of scientific information and DNA/RNA sequences likely will give way to a very intensive and aggressive patent strategy for research, development and commercialization of products derived from synthetic biology.[20]

The CF cannot, of course, resolve the complicated debate and litigation over patent thickets, foundational patents and their licensing for commercial products, much less the debate over whether the patenting of in *silico* DNA sequences should be allowed to act as a gatekeeper for what scientific researchers can do.[21] Nevertheless, a revised CF that authorizes Federal agencies to develop policies to limit the granting of CBI claims to cover trade secrets only, can prevent claims that health and safety data are proprietary from impeding robust peer-review of the applicant's science.

Conclusion

Revising the CF to enable Federal agencies to carry out their statutory duties to protect human, animal, plant and environmental health and life when regulating products of biotechnology is an urgent public policy priority that has been delayed far too long. IATP hopes that this revision will not be further delayed beyond the end of the Obama administration.

Endnotes

1. http://www.gpo.gov/fdsys/pkg/FR-2015-10-16/pdf/2015-26311.pdf

2. The Institute for Agriculture and Trade Policy (IATP) is a nonprofit, 501(c)(3) nongovernmental organization, headquartered in Minneapolis, Minn., with an office in Washington, D.C. Our mission states, "The Institute for Agriculture and Trade Policy works locally and globally at the intersection of policy and practice to ensure fair and sustainable food, farm and trade systems."

3. Cited in William Freese and David Schubert, "Safety Testing and Regulation of Genetically Engineered Foods," Biotechnology and Genetic Engineering Reviews – Vol. 21, November 2004, at 6. http://www.centerforfoodsafety.org/files/freese_safetytestingandregulationofgeneticallyebgineeredfoods_nov212004_62269.pdf

4. E.g. David Schultz's interview with Phil Miller, Monsanto's vice president for global and regulatory affairs, Chemical Regulation Reporter, Bloomberg BNA, November 9, 2015.

5. "Environmental Effects of Transgenic Plants: Scope and Adequacy of Regulation, National Research Council , 2002, cited in EC Biotech Products, "Amicus Curiae Brief," Center for International Environmental Law et al., (June 1, 2003), paragraph 10.

6. Trudy Lieberman, "Today's federal agencies are 'highly message controlled: Here's what that means for health reporting," Columbia Journalism Review, November 10, 2015. http://www.cjr.org/the_second_opinion/health_reporting_obama_administration.php

7. Andrea L. Halweg Edwards et al., "The emergence of commodity-scale genetic manipulation," Current Opinion in Chemical Biology (2015) 28: 150-156. http://dx.doi.org/10.1016/j.cbpa.2015.07.009

8. Sarah R. Carter et al., "Synthetic Biology and the U.S. Biotechnology Regulatory System: Challenges and Options," J. Craig Venter Institute, May 2014, 24. http://www.jcvi.org/cms/fileadmin/site/research/projects/synthetic-biology-andthe-us-regulatory-system/full-report.pdf .

9. http://ec.europa.eu/health/scientific_committees/emerging/docs/scenihr_o_048.pdf at 6.

10. Oliver Wright, Guy-Bart Stan and Tom Ellis, "Building-in biosafety for synthetic biology," Microbiology 159 (July 2013), 1223.

11. Ibid., 1227.

12. E.g. Joan Murphy, "Food industry urges OMB, HHS not to revert to FSMA user fees in FY 2017 FDA budget plan," Food Chemical News, August 28, 2015 and Ronald White, "Congress' Latest Assault on the EPA," Center for Effective Government, July 14, 2014. http://www.foreffectivegov.org/blog/congresss-latest-assault-epa.

13. Lynn Bergeson et al., "The DNA of the U.S. Regulatory System: Are We Getting It Right for Synthetic Biology?" Woodrow Wilson Center Project on Synthetic Biology, October 2015, 41-43. http://www.synbioproject.org/publications/dna-of-the-u.s-regulatory-system/.

14. "The Rise of Superweeds and What to Do About It," Union of Concerned Scientists, 2013. http://www.ucsusa.org/sites/default/files/legacy/assets/documents/food_and_agriculture/rise-of-superweeds.pdf .

15. Werner Arber, "Horizontal Gene Transfer among Bacteria and Its Role in Biological Evolution," Life, June 2014, 224. http://www.ncbi.nlm.nih.gov/pmc/articles/PMC4187160/

16. National Academy of Sciences and National Research Council, Safety of Genetically Engineered Foods: Approaches to Assessing Unintended Health Effects. National Academy Press, 2004, at 10. http://www.nap.edu/read/10977/chapter/2#10

17. Sapna Kumar and Arti Rai, "Synthetic Biology: The Intellectual Property Puzzle," Texas Law Journal Vol. 85 (2007), 1751. http://scholarship.law.duke.edu/cgi/viewcontent.cgi?article=2327&context=faculty_scholarship

18. Kaare M Nielsen, "Biosafety Data as Confidential Business Information," PLOS Biology 11(3) (March 2013), 1. http://journals.plos.org/plosbiology/article?id=10.1371/journal.pbio.1001499

19. "Modernizing the Regulatory System for Biotechnology Products," Office of the President, July 2, 2015. https://www.whitehouse.gov/sites/default/files/microsites/ostp/modernizing_the_reg_system_for_biotech_products_memo_final.pdf

20. Josie Garthwaite, "Beyond GMOs: The Rise of Synthetic Biology," The Atlantic, September 25, 2014. http://www.theatlantic.com/technology/archive/2014/09/beyond-gmos-the-rise-of-synthetic-biology/380770/

21. Bryn Nelson, "Synthetic Biology: Cultural Divide," Nature, May 7, 2014. http://www.nature.com/news/synthetic-biology-cultural-divide-1.15149