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Session: Science of Genetic Engineering
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THE SCIENCE OF GENETIC ENGINEERING: REGULATING THE NEXT GE REVOLUTION

This outline is a summary of anticipated opening remarks that will guide a dialogue between myself and Dr. Peter Goldsborough, Purdue University professor of botany plant pathology. For additional detail, including citations, on the legal background of federal biotechnology regulation and the advent of new technologies, see the attached excerpt from an article on the subject forthcoming in Valparaiso University Law Review.

1. Federal biotechnology regulation dates to the 1986 Coordinated Framework for the Regulation of Biotechnology. Coordinated Framework for Regulation of Biotechnology, 51 Fed. Reg. 23,302 (June 26, 1986).

    a. The Coordinated Framework divides federal regulatory authority between three agencies:

        i. The United States Department of Agriculture ("USDA"), which regulates the testing and commercialization of new agricultural biotech products;

        ii. The Food and Drug Administration ("FDA"), which regulates the introduction and marketing of foods created through the use of genetic engineering; and

        iii. The Environmental Protection Agency ("EPA"), which regulates genetically-altered microorganisms and pesticide properties of genetically-engineered plant varieties.

    b. Agency authority is based on several statutes that pre-existed genetic engineering.

        i. FDA's authority is based primarily on the Federal Food, Drug and Cosmetic Act ("FDCA"), which gives FDA authority to regulate food additives and misbranding. Ch. 675, 52 Stat. 1040 (1938) (codified as amended 21 U.S.C. §§ 301-399f (2012)).

        ii. USDA's authority stems primarily from the Plant Protection Act, which gives USDA authority to regulate plant pests and noxious weeds. 7 U.S.C. §§ 7701-7786 (2012).

        iii. EPA's authority derives primarily from the Federal Insecticide, Fungicide and Rodenticide Act ("FIFRA"), which gives EPA authority to regulate pesticides, and the Toxic Substances Control Act ("TSCA"), which gives EPA authority to regulate new microorganisms. FIFRA, Ch. 125, 61 Stat.

163 (1947) (codified as amended at 7 U.S.C. §§ 136-136y (2012)); TSCA, Pub. L. No. 94-469, 90 Stat. 2003 (1976) (codified as amended in scattered sections of 15 U.S.C. (2012)).

2. The Coordinated Framework presumed that biotechnology would involve transgenic organisms, or organisms in which genetic material from another, non-sexually compatible organism has been inserted into the target organism.

    a. Transgenic organisms were considered "plant pests" under the PPA because scientists used viruses or bacteria as vectors to insert the transgenic material.

    b. Transgenic material was considered a "food additive" under the FDCA because it was inserted from a different organism. However, transgenic material was presumed to be GRAS and therefore not subject to pre-market safety review under the FDCA. FDA established an alternative voluntary pre-market consultation process for biotechnology products.

3. However, the next generation of biotechnology products does not fit the presumptions upon which the Coordinated Framework was based.

    a. New technology for creating transgenic organisms does not rely on bacteria or viruses as vectors. Alternatives include a "gene gun," in which metal pellets coated with DNA are fired into the target organism.

    b. New technologies in some cases do not create transgenic organisms at all. Instead of inserting material, techniques like the CRISPR/Cas9 system directly modify or delete genes from the target organism's genetic code.

    c. Some technologies more efficiently combine DNA from sexually compatible relatives, which could theoretically have cross-bred in nature.

4. New genetic engineering techniques are or may be unregulated by federal agencies because they exceed the scope of the agencies' statutory authority.

    a. USDA has already informed dozens of producers of new biotechnology products that USDA lacks jurisdiction over their products because they do not utilize plant pests. *See* National Academy of Science, Genetically Engineered Crops: Experiences and Prospects 330 (2016) (Table 9-3).

    b. Genetically-engineered organisms that do not involve insertion of any genetic material arguably may not fall within FDA's jurisdiction over "food additives."

5. CRISPR is predicted to cause a revolution in biotechnology.

    a. In August 2016, *National Geographic* published an article about new genetic engineering techniques entitled "DNA Revolution." The article's tag line read:

"The ability to quickly alter the code of life has given us unprecedented power over the natural world. The question is: Should we use it?"

b. CRISPR has been studied for a wide range of applications, including agriculture, human health, and human genetic enhancement.

   i. In agriculture, for example, researchers are working to use genome editing techniques to introduce into dairy cattle a genetic variant that causes cattle to lack horns, avoiding the need for dehorning.

   ii. In medicine, genome editing is being used to explore the possibility of knocking out the gene for CCR5, the functional co-receptor in T cells used by the HIV-1 virus.

   iii. The combination of CRISPR technology and a natural system called a gene drive has allowed scientists to attempt the manipulation of the DNA of mosquitos carrying diseases like malaria and Zika so that they give birth to sterile offspring, wiping out the disease-carrying population within a few generations.

c. Secondary effects of genome editing modifications are not understood, however.

   i. Sterilization of whole populations within a few generations could cause unknown consequences such as proliferation of other pests.

   ii. CRISPR could be also be used to engineer "designer humans."

d. CRISPR is inexpensive and easy for even the smallest labs to access and use and could lead to an explosion of new technologies in the near future.

e. Influential scientists, including a Nobel Prize winner and the scientists who published the discovery of the CRISPR/Cas9 system, have called for a temporary moratorium on application of the technology to discuss ethical and legal controls. *See* David Baltimore et al., *A Prudent Path Forward for Genomic Engineering and Germline Gene Modification*, 348 SCIENCE 36 (2015).

6. The Obama Administration has recognized the growing incongruence between the Coordinated Framework and new genetic engineering techniques.

   a. The Obama Administration has commissioned an inter-agency task force to study the issue and make recommendations, due to be released in the summer of 2016.

   b. It is unclear whether the new technologies can be reached and effectively regulated by the agencies' existing statutory authority. New legislation may be required.

7. The prospect of a genetic engineering revolution raises a number of questions for federal legislators and regulators, including the following:

    a. Are existing statutes sufficient to regulate genetic engineering or is new legislation required?

    b. How should "genetic engineering" be defined in the law? Should all new genetic engineering techniques be included and regulated together?

    c. Should the regulation of genetic engineering be consolidated in a single federal agency?

    d. Federal regulation is currently based on whether a product of genetic engineering fits into a certain category: a plant pest, food additive, microbe, pesticide, etc. Should regulation move to either a process-based approach, in which all genetically-engineered products are regulated regardless of risk, or a product-based approach, in which only products posing unique or unknown risks are regulated?

    e. What kind of assessment process might allow regulators to distinguish between low-, moderate-, and high-risk products of genetic engineering?

    f. Are products of genome editing safer than transgenic organisms? Less safe? Does the answer depend on the product or technique?

    g. Does the PPA over-regulate well-understood risks by relying on the "plant pest" definition?

    h. Are non-transgenic genetically-engineered organisms subject to "food additive" jurisdiction by FDA?

    i. Does the GRAS presumption by FDA provide for a sufficient risk assessment of new genetically-engineered products?