

CRISPR-edited crops free to enter market, skip regulation

The first CRISPR-edited crops presented to the US regulatory system can be cultivated and sold without oversight by the US Department of Agriculture (USDA), the agency said in a pair of letters posted in April. The decisions could reduce by millions the cost of development of the crops: an anti-browning mushroom and a waxy corn genetically modified with the gene editing tool CRISPR-Cas9. Some scientists hailed the decision as a step in the right direction, although media outlets and other interested parties said it illustrates the murky state of US biotech regulations.

Johnston, Iowa-based DuPont Pioneer engineered the waxy corn to contain starch composed exclusively of the branched polysaccharide amylopectin—a component in processed foods, adhesives and high-gloss paper. Company researchers achieved the effect by shutting down production of cornstarch's other long-chain polysaccharide, amylose. Using the gene-editing tool CRISPR-Cas9, the team knocked out the endogenous waxy gene *Wx1*, which encodes the endosperm's granule-bound starch synthase responsible for making amylose.

DuPont Pioneer, currently undergoing a merger with The Dow Chemical Company, says it expects the CRISPR-edited variety to have higher yields than conventional waxy corn. The company plans to commercialize the plant within five years and follow it with many more CRISPR-edited crops. "This is just the beginning," said Neal Gutterson, vice president of R&D, in a statement released to coincide with the USDA's response.

Pioneer previously partnered with Vilnius University in Lithuania and Berkeley, California-based Caribou Biosciences to advance CRISPR-Cas techniques, and is open to other collaborations to apply the tool across all crops and geographies, Gutterson said. The company licensed CRISPR-Cas from Vilnius and Caribou, but ownership of the intellectual property rights to CRISPR-Cas is under review by the US Patent and Trademark Office's Patent Trial and Appeal Board (*Nat. Biotechnol.* **32**, 599–601, *Nat. Biotechnol.* **34**, 121, 2016)

Commercial plans for the gene-edited mushroom remain less clear. Yinong Yang, a plant pathologist at Pennsylvania State University (Penn State) in University Park, engineered the crop, a common white button variety (*Agaricus bisporus*). Yang used CRISPR-Cas9 to engineer the fungus to have anti-browning properties. The trait increases the mushroom's visual appeal and shelf life.

Yang achieved the effect by knocking out one of the six genes that encode polyphenol oxidase (PPO), an enzyme that causes browning in many fruit and vegetables. PPO has been targeted by companies developing non-browning apples (*Nat. Biotechnol.* **33**, 326–327, 2015) and potatoes (*Nat. Biotechnol.* **33**, 12–13, 2015). Yang says he and his university have not yet decided whether they will commercialize the mushroom.

Yang's mushroom and DuPont's corn don't require USDA oversight because they do not contain genetic material from plant pests such as viruses or bacteria—a common and, until recently, a



DuPont Pioneer's high amylopectin corn is the first CRISPR-edited plant likely to bypass USDA oversight.

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necessary tool in biotech. Plant pests have served as the trigger for USDA oversight since the 1980s, when the US government wrote the regulatory framework for biotech products.

Newer genetic engineering (GE) techniques that don't involve plant pests are quickly supplanting the old ones, and the USDA appears to be saying it does not have the authority to regulate the products of these techniques. The letters to DuPont and Yang were the agency's first decisions on CRISPR-edited crops. The agency ruled similarly on plants transformed with other gene-editing techniques, such as zinc-finger nuclease and transcription activator-like effector nuclease systems.

Such letters from USDA have become "essential" to small companies attempting to bring to market GE plants, says Antony Evans, CEO of the San Francisco-based startup TAXA Biotechnologies. The company in 2014 received a letter for its bioluminescent glowing plant technology. "If you don't get a letter like that, it's very hard to...raise any money" because investors are leery of going through the cost-prohibitive regulatory process, he says.

Crops that bypass the USDA may still go through the voluntary review process at the US Food and Drug Administration (FDA). And the US Environmental Protection Agency (EPA) reviews crops with certain traits such as insecticidal properties.

In an effort to catch up with technology, the White House has ordered the USDA, the FDA and the EPA to update the system, known as the Coordinated Framework for the Regulation of Biotechnology (*Nat. Biotechnol.* **33**, 1221–1222, 2015). To that end, the agencies in the last year have held three public meetings, including two in March. Many groups weighed in at those meetings and in the literature. The USDA in parallel is updating its own regulations. A public comment period for that ended April 21.

The agencies enlisted help from a committee convened by the US National Academies of Sciences, Engineering and Medicine. The committee will attempt to predict "the likely future products of biotech over the next 5–10 years" and what types of risks those products might pose, according to the committee's charge. The group met for the first time on April 18 and plans to publish a report by the end of 2016.

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