



# CRISPR Q&A – For Internal Use Only May 28, 2019

#### **Contents**

Key Messages	1
Available Resources	
Questions We Can't Answer at this Time	
Basic CRISPR	
Safety	
Relationship to GMOs	
Regulatory	9
Next Generation Waxy Corn and Other CRISPR Products in Development	13
Social License and Public Acceptance	17
Open Innovation and Intellectual Property	18
Human Medicine	21

Corteva Agriscience™ is excited to tell its CRISPR story and play an active role in facilitating understanding of the technology and its benefits by growers, customers, consumers, media and other key influencers. Questions about CRISPR from the public will continue to grow, giving us an opportunity to tell our story effectively, highlight CRISPR benefits and correct misperceptions.

This document is a guide for verbal discussions. Do not forward or share with external audiences in written format. Please check with Ashlee Stoddard (ashlee.stoddard@pioneer.com or +1-515-829-7687) to ensure you are using the most up-to-date information.

## **Key Messages**

We need to grow food that is better for people and the environment. To accomplish this goal, we must explore innovations and new technologies, including CRISPR.

Agriculture is at a crossroads. Plants are under attack from changing weather, drought, floods, heat
waves, diseases and pests. At the same time, our population is growing and consumers are increasingly
demanding food that is healthier for their families and the planet. This means we need to grow more
food that is better for people and the environment using fewer resources.





- CRISPR-produced seeds help us grow healthy and nutritious food that is better for people and the
  environment.
- CRISPR gene editing can create an improved plant that does not include DNA from a different species.
   CRISPR makes it possible to deliver nutritious plants that could occur in nature or be developed through conventional breeding, but faster and more efficiently.
- CRISPR has the potential to produce many consumer benefits.
  - Crops that taste better and have more vitamins and nutrients for people and animals.
  - Less expensive food due to fewer resources needed to grow them.
  - Reduced food waste due to fruits and vegetables that don't brown or rot quickly.
- Researchers can use CRISPR gene editing to make specific and exact changes in a plant by deleting,
  editing or moving a gene in the plant's own DNA. The principles used to achieve positive
  characteristics in plants with CRISPR are the same as those used in traditional plant breeding for
  conventional and organic crops, but applied more exactly and more quickly.
- CRISPR-produced plants are as safe as plants found in nature or produced through conventional breeding or GMO technology.
  - Exact Changes: The nature of CRISPR technology is that it makes very specific, targeted changes. These changes could occur in nature or be developed through conventional breeding, but CRISPR makes it possible to deliver them faster and more efficiently.
  - **Extensive Testing:** At Corteva Agriscience<sup>TM</sup>, CRISPR-produced seeds are extensively field-tested to ensure that the specific changes to a plant's own DNA have been made exactly as intended.
  - If Pressed, Specific Details on Testing: We conduct thousands of field tests over several years
    to study a plant's various growth characteristics, appearance, yield, and resistance to diseases
    and pests to confirm that edited plants grow and perform as intended.
    - 1. Researchers confirm the intended change was successful.
    - 2. Researchers conduct field tests of thousands of plants over several years to confirm that plants grow and perform as intended.
    - 3. Corteva engages routinely with regulatory agencies like the FDA about our products. We adhere to all FDA food safety regulations for all our products.
    - 4. Researchers are using CRISPR to discover treatments and cures for serious genetic diseases and conditions, such as certain types of cancer, sickle cell anemia, cystic fibrosis and early-onset Alzheimer's advances that could improve the lives of millions.
- Corteva is committed to making information about CRISPR and how it is being used to produce seeds transparent and available to the public.





• Corteva Agriscience™ is committed to encouraging broad adoption of this technology in agriculture by enabling access to its CRISPR intellectual property rights for nonprofit organizations, academics and commercial enterprises with the intent to solve local food challenges with local solutions.

#### **Available Resources**

In addition to this Q&A, spokespeople should refer to the companion document "CRISPR Research Insights and Messaging" for key messages about CRISPR independent of specific questions or situations.

Approved videos, infographics and other key materials are available to share externally depending on need and audience.

## **Questions We Can't Answer at this Time**

- Pricing strategy of products developed with CRISPR
- Specific branding or packaging of products developed with CRISPR
- Number of Corteva employees working on CRISPR
- Total investment in CRISPR
- Confirmation of any specific products or traits in development beyond the next generation of Waxy
   Corn hybrids and Northern Leaf Blight disease resistance for corn

#### **Basic CRISPR**

#### What is CRISPR?

CRISPR gene editing can create an improved plant that does not include DNA from a different species. CRISPR makes it possible to deliver nutritious plants that could occur in nature or be developed through conventional breeding, but faster and more efficiently. CRISPR-produced plants are as safe as plants found in nature or produced through conventional breeding or GMO technology.

#### How does CRISPR work?

CRISPR works much like editing text on a computer. Researchers use CRISPR gene editing to make specific and exact changes in a plant by deleting, moving or editing a plant's own DNA to achieve a specific characteristic such as drought resistance, disease tolerance or improved nutritional value.





Researchers can achieve the same positive characteristics in plants with CRISPR as in conventional and organic crops developed through traditional plant breeding, but more exactly and more quickly.

### Why do we need CRISPR in agriculture?

Agriculture is at a crossroads. Plants are under attack from changing weather, drought, floods, heat waves, diseases and pests. At the same time, our population is growing and consumers are increasingly demanding food that is healthier for their families and the planet. This means we need to grow more food that is better for people and the environment using fewer resources. To accomplish this goal, we must explore new innovations and technologies – and CRISPR is one of these innovations.

## What are the potential benefits of CRISPR in agriculture?

CRISPR can help us grow food that is better for people and the environment.

**Consumers:** Potential consumer benefits include crops that taste better and have more vitamins and nutrients, food that is less expensive due to the use of fewer resources to grow crops, and less food waste due to fruits and vegetables that do not brown or rot quickly.

**Environment:** Potential environmental benefits include reducing the amount of water and land needed to grow crops as well as creating plants that can use fewer pesticides and more "green chemistry" to grow. Green chemistry, also known as sustainable chemistry, is the design of chemical products and processes that reduce or eliminate the generation of hazardous substances.

**Farmers:** Potential farmer benefits include crops that are pest and disease resistant, have higher yields, are better able to withstand weather conditions like drought, and need fewer inputs like water or fertilizers.

## What particular type of CRISPR technology are you using?

Currently, Corteva Agriscience™ uses CRISPR-Cas9 technology.

#### To which crops can CRISPR technology be applied?

CRISPR has broad application to crops, including fruits and vegetables.

#### How is CRISPR technology applied beyond plants/agriculture?

It also has potential applications for human medicine. Researchers are using CRISPR to discover treatments and cures for serious genetic diseases and conditions, such as certain types of cancer, sickle cell anemia, cystic fibrosis and early-onset Alzheimer's – advances that could improve the lives of millions.





#### Safety

## Is the use of CRISPR in agriculture safe?

Yes. CRISPR can be used in agriculture to deliver plants that are as safe as plants found in nature or produced through conventional breeding or GMO technology. Corteva Agriscience™ rigorously tests CRISPR-produced seeds to confirm the intended changes are made to a plant's own DNA and the resulting plants perform as expected.

## How do you know there will not be unintended consequences or off-target issues?

CRISPR enables specific and exact changes to a plant's DNA compared to conventional breeding methods. In addition, Corteva field-tests CRISPR-produced crops extensively to confirm specific changes are made exactly as intended.

## How are CRISPR plants tested?

Corteva tests all the plants we develop to confirm changes were made as intended. Specifically, for CRISPR-produced plants:

- Corteva researchers confirm the intended change was successful.
- Corteva researchers conduct field tests of thousands of plants over several years to confirm that plants grow and perform as intended.
- Corteva engages routinely with regulatory agencies like the FDA about our products. We adhere to all FDA food safety regulations for all our products.

#### Are CRISPR plants tested like other plants?

Yes, Corteva extensively field-tests CRISPR-produced plants the same way we test our conventionally bred plants, which involve detailed observations of the plant's various growth characteristics, appearance, yield, and resistance to diseases and pests.

#### Why aren't CRISPR plants tested more than conventionally bred plants?

CRISPR-produced plants, like conventionally bred plants, do not include DNA from a different species. Therefore, the CRISPR-produced plants that advance to the testing stage can be tested the same way as plants bred conventionally.





## Isn't it possible that someone could use CRISPR to create a plant that is dangerous for people, animals or the environment?

History has shown us that any technology can be used to create both positive and adverse effects. But the market demand is for more food that is healthy for people and the environment, grown more quickly and efficiently – and that is what CRISPR makes possible.

# How do you know these CRISPR-produced plants are safe for human consumption over the long term? What human health studies are you conducting?

Corteva Agriscience™ uses CRISPR to produce plants more quickly that could occur in nature or be produced by conventional breeding. This gives us confidence that CRISPR plants are as safe as these other kinds of plants, which have been consumed safely by humans for hundreds of years.

#### But there could be off-target DNA changes in CRISPR plants, right?

CRISPR uses detailed knowledge of a plant's DNA to introduce targeted, specific changes. Because of this targeting, researchers can make these exact DNA changes with fewer additional DNA changes than what would occur in nature or with conventional breeding. In this way, CRISPR can reduce potential off-target DNA changes in CRISPR-produced plants.

Every plant – whether found in nature, created by conventional breeding methods in use for hundreds of years, or produced with technologies like CRISPR – has DNA that changes with every generation. It is inaccurate to say that changes in DNA result only from technologies like CRISPR.

Further, when Corteva creates a new CRISPR-produced seed, we field-test thousands of plants over several generations and growing locations, making detailed observations of the plant's various growth characteristics, appearance, yield, and resistance to diseases and pests. This is a standard practice to monitor that plants perform as expected before commercialization.

#### Do you do tests to confirm the safety of CRISPR?

Corteva tests CRISPR-produced plants the same way we test our conventionally bred plants, which involve detailed observations of the plant's various growth characteristics, appearance, yield, and resistance to diseases and pests. This is a standard practice to monitor that plants perform as expected before commercialization.





## **Relationship to GMOs**

NOTE: All discussions comparing CRISPR to GMOs should start with the premise of why such innovations are needed today.

Agriculture is at a crossroads. Plants are under attack from changing weather, drought, floods, heat waves, diseases and pests. At the same time, our population is growing and consumers are increasingly demanding food that is healthier for their families and the planet. This means we need to grow more food that is better for people and the environment using fewer resources. To accomplish this goal, we must explore new innovations and technologies – and CRISPR is one of these innovations.

## Are CRISPR plants GMOs?

No, CRISPR-produced plants are not GMOs. "GMO" is a term that is traditionally used to refer to transgenic plants. "Transgenic" means that the plant includes DNA from a different species. This transgenic DNA is inserted into the plant's own DNA via genetic engineering to create a GMO, or transgenic plant.

In contrast, researchers can use CRISPR to create an improved plant that does not include DNA from a different species. CRISPR allows us to make specific changes in a plant by deleting, editing or moving a plant's own DNA – improvements that could occur in nature or be developed through conventional breeding.

If CRISPR were used to create a plant that includes DNA from a different species, that plant would be a GMO.

#### Are CRISPR-produced plants safer than GMOs?

This question reflects a common misperception about GMOs. GMOs are subjected to rigorous testing prior to commercialization. Since this testing was put in place three decades ago, the safety of GMOs has been validated by numerous government regulatory bodies and credible scientific bodies around the world.

CRISPR-produced plants are as safe as plants produced through GMO technology or conventional breeding or plants found in nature.

## Why aren't CRISPR-produced plants regulated like GMOs?

Global regulatory policies for CRISPR crops are still in development in many countries, with countries starting to provide more policy clarity.

CRISPR can be used to produce plants that do not include DNA from a different species, and their characteristics could occur in nature or through conventional plant breeding. Therefore, we believe they should be regulated the same as plants produced through conventional breeding methods.





If CRISPR were used to create a plant that includes DNA from a different species, that plant would be a GMO.

#### Is CRISPR more "natural" than GMOs (transgenics)?

The changes to a plant's DNA made possible by CRISPR could also occur in plants found in nature or produced by conventional breeding. CRISPR simply enables these principles to be applied more exactly and more quickly.

Every plant – whether found in nature, created by conventional breeding methods in use for hundreds of years, or produced with technologies like CRISPR or GMO – has DNA that changes with every generation. Even what we think of as "natural" plants are continuing to change over time, similar to the ways that technology can change plants, so one could argue CRISPR-produced plants are similarly "natural."

## How do CRISPR-produced compare to GMO (transgenics) plants in nutritional profile (vitamin/mineral content)?

One of the possible benefits of CRISPR is to produce plants that are more nutritious than those found in nature or produced by conventional breeding. Ultimately, the plant's nutritional profile will depend on what characteristics researchers, companies and universities develop and commercialize.

CRISPR gene editing, conventional genetic engineering and traditional breeding can be used to change the nutritional profile of a plant if desired. So, it is possible that a CRISPR-produced plant could be more nutritious than a GMO (as well as plants found in nature or bred conventionally). Similarly, a GMO plant could be created to have a better nutritional profile than other plants.

## Will Corteva Agriscience™ use CRISPR to replace GMOs?

Corteva develops and uses many tools, including CRISPR, to develop new seeds to help farmers grow healthy food for more people, with less land and fewer resources. Corteva will continue to provide a variety of seed options, including those developed from conventional, GMO and CRISPR methods, so that farmers and consumers have choices.

CRISPR can be used to improve a plant's characteristics without including DNA from a different species. That means we can develop improvements that are no different than those that could occur in nature or through conventional breeding over decades, except that CRISPR makes it possible to deliver the same benefits in a few years and just as safely.

Both GMO and CRISPR tools are important for agriculture today. Plants are under attack from changing weather, drought, floods, heat waves, diseases and pests. At the same time, our population is growing and





consumers are increasingly demanding food that is healthier for their families and the planet. This means we need to grow more food that is better for people and the environment using fewer resources. To accomplish this goal, we must explore new innovations and technologies – CRISPR is one of these innovations.

#### Regulatory

#### How are CRISPR-produced plants regulated in the U.S.?

Three federal agencies regulate products of food and agricultural technology. Together, United States Department of Agriculture (USDA), the Environmental Protection Agency (EPA) and the Food and Drug Administration (FDA) work under the Coordinated Framework for the Regulation of Biotechnology to ensure these products are safe for the environment and human health.

USDA's regulations focus on protecting plant health; FDA oversees food and feed safety; and EPA regulates the sale, distribution, and testing of pesticides to protect human health and the environment.

 In March 2018, USDA stated that it "seeks to allow innovation when there is no risk present" and clarified its policy towards plant breeding innovations, stating that:

"Under its biotechnology regulations, USDA does not currently regulate, or have any plans to regulate, plants that could otherwise have been developed through traditional breeding techniques as long as they are developed without the use of a plant pest as the donor or vector and they are not themselves plant pests."

Therefore, if a CRISPR produced plant is indistinguishable from one developed through traditional breeding methods and meets the plant pest criteria above, such CRISPR-produced plants are regulated in the same way as all traditionally bred plants are regulated (e.g., Federal Seed Act under USDA APHIS and AMS, state Seed laws, etc.).

FDA's 1992 policy ("Statement of Policy: Foods Derived from New Plant Varieties") established a
process by which companies can voluntarily consult with the FDA about food safety prior to marketing
new plant varieties, to address any questions related to regulatory status.

FDA policy is not specific to any technology by which the new food crop is produced.

Importantly, the existing FDA laws and regulations require everyone in the farm-to-table continuum to market safe foods to consumers, regardless of the process by which such foods are created.





EPA's scope of regulatory oversight is for pesticides, and specific to plants, plant-incorporated
protectants (PIPs) – in other words, substances produced and used in living plants that can prevent,
destroy, repel, or mitigate any pest. Hence, not all CRISPR-produced plants will have characteristics
that fall under EPA oversight in the first place.

In September 2016, EPA stated that it "intends to clarify its approach to pesticidal products derived from genome editing techniques" but a formal policy clarification for CRISPR-produced crops has not yet been announced.

EPA has long recognized that products of conventional breeding have a solid record of safety for human health and the environment, and specifically exempted PIPs developed through conventional plant breeding from regulation. Since publishing its proposed rule in 1994, EPA has consistently stated its intent to focus its regulatory efforts on those pesticidal substances "that are new to the plant" and "have greater potential for environmental and/or human health risks" and those "isolated from novel sources" that "may present novel, unknown and/or unfamiliar toxicological profiles."

## Position on EPA regulation (for technical audiences):

If a CRISPR-produced crop produces a PIP using genetic material "from a plant that is sexually compatible with the recipient plant" – that is, if the plant does not contain DNA from another species – it meets EPA's conventional breeding exemption described above. Note that EPA oversight remains in place for plants that fall under the conventional breeding exemption - they are not exempt from adverse effect reporting obligations.

Deviating from this policy and existing regulations to address gene editing would undermine innovation, needlessly expand Agency oversight, and run counter to a policy that "limits EPA's regulatory role in conventional plant breeding and ensures that the Agency does not unnecessarily supplant the self-regulating aspects of plant breeding."

#### How are CRISPR-produced plants regulated outside the U.S.?

Global regulatory policies for CRISPR crops are still in development in many countries, with countries gradually starting to provide clarity on this matter. Regulators in Argentina, Brazil, and Chile confirmed that if no DNA from another species is present in the plant, such plants will not be considered as GMO under their country's law.

Note: Please contact your local regulatory expert to learn about the regulatory policies in your country.

*Is the regulatory system for CRISPR-produced crops clear?* 





Corteva Agriscience™ continuously monitors the development of global regulatory policies for products of CRISPR technology and is in regular consultation with global regulatory bodies and government agencies. We continue to encourage a science-based approach and believe that regulatory oversight should focus on the characteristics of the product – not the process by which it is created.

#### Does CRISPR shorten the amount of time it can take to get a new product to market?

We are hopeful that it will. It does shorten the product development lifecycle because CRISPR-produced plants can be developed in just a few years versus what often takes decades. However, introducing a new product involves factors such as harmonization of global regulations.

CRISPR-produced plants do not include DNA from a different species and should not be subject to the same onerous and lengthy regulatory approval process that has been historically put in place for GMOs. Treating CRISPR-produced crops as GMOs would substantially slow down their path to market and adoption of CRISPR innovation in agriculture.

## What impact will CRISPR have on agriculture in developing countries?

People living in developing countries across the globe have a particular need for access to more food that is healthier for people and the environment and produced with fewer resources. CRISPR is one tool that can help meet this need. It can be applied to a wide variety of crops, including local staple food crops, fruits and vegetables, addressing critical local agriculture challenges.

Corteva is committed to encouraging broad adoption of this technology in agriculture by enabling access to its CRISPR intellectual property rights for nonprofit organizations, academics and commercial enterprises with the intent to solve local food challenges with local solutions.

#### Shouldn't there be more regulation of CRISPR-produced plants?

CRISPR-produced plants do not include DNA from different species, and their characteristics could occur in nature or through conventional plant breeding. Therefore, we believe they should be regulated the same as plants produced through conventional breeding methods.

Regulatory policies should be cost effective and commensurate with the risk. They should be transparent, consistently applied and enforced, and globally harmonized.

Why aren't CRISPR-produced seeds regulated by the USDA's biotechnology regulatory services?





USDA's Biotechnology Regulatory Services regulates plants that are or may be plant pests, regardless of the production technique. Therefore, when CRISPR is used to develop a plant not meeting these criteria, such CRISPR plants will not be regulated by USDA BRS. CRISPR-produced plants will still be subject to all the same regulations applied to conventionally bred plants.

Given a huge interest in CRISPR technology and a rising number of applications to develop CRISPR crops, in March 2018 USDA issued a special clarification of its policy towards plant breeding innovations. In summary:

"Under its biotechnology regulations, USDA does not currently regulate, or have any plans to regulate plants that could otherwise have been developed through traditional breeding techniques as long as they are developed without the use of a plant pest as the donor or vector and they are not themselves plant pests."

#### In the U.S., does the FDA need to be consulted to bring a CRISPR-produced plant to market?

The FDA does not need to be consulted. However, Corteva Agriscience™ engages routinely with regulatory agencies like the FDA on our products. FDA's 1992 policy ("Statement of Policy: Foods Derived from New Plant Varieties") established a process by which companies can *voluntarily* consult with the FDA prior to marketing new plant varieties, to address any questions related to regulatory status. This policy is not specific to any technology by which the new plant variety is produced. Importantly, the existing FDA laws and regulations require everyone in the farm-to-table continuum to market safe foods to consumers, regardless of the process by which such foods are created.

#### What is the view of Corteva on the European Court of Justices' decision?

We are disappointed that the European Court of Justice interpreted the provisions in the EU's GMO Directive in such a way that plants developed with innovative, targeted mutagenesis technologies should be treated as GMOs and subject to the respective onerous regulatory provisions in the EU.

The Court's decision effectively cuts off European plant breeders, researchers and innovators from scientific progress. Subjecting plant breeding innovations to undue regulatory burden will have a direct effect on efforts to build a more sustainable and resilient agriculture by depriving European farmers, consumers and the wider agri-food chain, of a range of important benefits.

The Court's decision is also contrary to the views taken by regulatory bodies outside of Europe, who have examined the science and concluded that plant varieties developed through the latest breeding methods should not be subject to different or additional regulatory oversight if they could also be obtained through earlier breeding methods or found in nature.

While the ruling is disappointing, it did not come as a complete surprise, as the EU has traditionally taken a precautionary approach to new agricultural technologies. We strongly encourage the incoming EU policy





makers to provide more workable legislation that would allow farmers and consumers across Europe to take advantage of the many benefits that plant breeding innovations, such as CRISPR, can offer.

## Are you collaborating with any European firms on CRISPR as part of your Open Innovation initiative or otherwise?

Corteva Agriscience™ remains committed to CRISPR. We must keep innovating, testing and improving to solve the world's toughest food challenges. That's how we will fulfill our mission of enriching the lives of those who produce and those who consume, ensuring progress for generations to come.

We are in discussions with several European groups and welcome other interested organizations to contact us via our Open Innovation website: OpenInnovation.Corteva.com.

#### **Next Generation Waxy Corn and Other CRISPR Products in Development**

Note: All comments about Waxy Corn should be checked with the team to confirm that you have the most accurate and up-to-date information.

## What is CRISPR-produced Waxy Corn?

Corteva's CRISPR-produced Waxy Corn is a more sustainable starchy corn that improves yield so farmers can produce more corn starch using the same land and resources. Waxy Corn produces starch for industrial applications, such as bottle labels, and for food thickening agents, such as corn starch.

#### What is the status of Waxy Corn?

Corteva will launch phase one of our commercial pilot of CRISPR-produced Waxy Corn for the U.S. market in the 2019 growing season.

#### Will you sell Waxy Corn for the coming season?

No. This is phase one of a commercial pilot, not a commercial launch. We are not selling CRISPR-produced seeds at this time.

#### Didn't you say you would start selling it this year? Why the delay?

The 2019 commercial pilot is moving ahead as expected. The commercial pilot has always been intended as an opportunity to solicit feedback, not as a commercial launch.





## If this is just a pilot, when will CRISPR-produced Waxy Corn seeds be for sale?

We cannot share this information until the pilot is completed, which will give us a clearer idea of the timing.

## What are your plans for Waxy next year?

We will have a clearer idea of plans for 2020 once phase one of the commercial pilot is complete.

## What do you expect to learn from the commercial pilot?

Corteva Agriscience<sup>TM</sup> expects to further confirm the benefits of CRISPR-produced Waxy Corn. These include improvements in yield, already shown in two years of extensive field trials conducted by our own researchers, and reduced resources required to grow Waxy Corn.

Additionally, we have committed to being open and transparent about our use of CRISPR technology and its safety. This pilot allows us to listen to the marketplace and to create a best-in-class transparency model for the industry.

## When will you see the financial return from CRISPR-produced Waxy Corn?

That is proprietary business information that we cannot discuss.

#### How will CRISPR-produced Waxy Corn be priced compared to non-CRISPR produced corn?

We are not selling CRISPR-produced seeds at this time, so it would be premature to discuss pricing.

## Will you monitor and trace grain from Waxy Corn?

The first phase of the CRISPR-produced Waxy Corn commercial pilot will include a handful of farmers and one processing partner.

Next generation Waxy Corn, just like existing Waxy Corn, will be identity-preserved during the entire process, from field to end-user. Identity preservation is needed because cornstarch produced from any Waxy Corn has unique benefits and, therefore, it does not make sense to mix Waxy Corn grain with the standard commodity corn grain used to produce cornstarch. Growers and processing partners will be required to implement stewardship practices specific to identity preservation systems; this will also ensure that next generation Waxy Corn will not be mixed into the commercial commodity corn grain stream shipped globally.

#### Who is your corn processing partner for CRISPR-produced Waxy Corn?





We are unable to disclose that information for competitive reasons.

### What Is the benefit of CRISPR-produced Waxy Corn? What is the point?

Our CRISPR-produced Waxy Corn will improve sustainability because farmers will get faster access to better, more modern and higher yielding corn hybrids having the waxy characteristic. We expect improvements in yield that are projected to reduce the resources needed to grow this crop and provide the supply stability strongly desired by waxy cornstarch processors.

# Why did Corteva Agriscience<sup>™</sup> select Waxy Corn rather than something with more direct consumer benefits?

We decided to start with a crop we know very well. With our 90-plus years of corn breeding experience, it was natural to bring our deep understanding of the biology of corn to our first commercial CRISPR-produced product.

We also have a great deal of experience with the Waxy characteristic in corn as an organization that has been selling conventional Waxy Corn hybrids since the mid-1980s and is the leading supplier of Waxy Corn in the United States.

Starting with this identity-preserved product as our initial CRISPR product offering allows us to lay a solid foundation for success for future larger-volume CRISPR products.

#### Does CRISPR-produced Waxy Corn have regulatory approval in the U.S. and beyond?

The Waxy Corn commercial pilot will be limited to the U.S. market. In the U.S. CRISPR-produced Waxy Corn is not subject to USDA biotech regulations. We confirmed this specifically with USDA in 2016 through the "Am I Regulated?" inquiry process.

### Will you label Waxy Corn?

Corteva is conducting this commercial pilot to solicit feedback prior to full commercialization. We are committed to making information about CRISPR and how it is being used to produce seeds transparent and available to the public and will communicate our position on labeling Waxy Corn once we make that determination.

## Will Corteva's CRISPR-produced Waxy Corn require GMO labeling if it appears in food products in the U.S.?

The characteristics in CRISPR-produced Waxy Corn could occur in nature or be produced with conventional breeding, which means that this product is not a GMO and therefore does not require that labeling.





## What other CRISPR-produced products does Corteva Agriscience<sup>TM</sup> have in development? What is the status of these products?

We are not yet ready to share our complete pipeline of CRISPR-produced products in development. We continue to develop seed products with CRISPR technology and have product concepts underway focused on disease resistance, healthier oil and improved feed quality.

As a specific example, Corteva is developing corn hybrids that are resistant to Northern Leaf Blight (NLB). NLB is a fungal disease that produces serious grain losses in the U.S., Brazil, Argentina, China and other parts of the world.

#### Does the delay of Waxy Corn change Corteva's commitment to CRISPR?

We remain committed to CRISPR technology and its potential to enrich the lives of those who produce and those who consume. Agriculture is at a crossroads, affected by many changes that range from environmental conditions to consumer preferences. Today's challenges require that we use all the tools at our disposal to identify and develop crops with added environmental and consumer benefits.

#### Can you share more about Corteva's CRISPR strategy beyond the Waxy Corn pilot?

Our vision is to use CRISPR to develop a variety of crops with added environmental and consumer benefits. We also know that no one company has all the answers to the challenges we face, so we are committed to encouraging broad adoption of this technology in agriculture by enabling access to our CRISPR intellectual property rights for nonprofit organizations, academics and commercial enterprises.

#### How will Cargill's new Waxy Corn Promise Program impact CRISPR-produced Waxy Corn at Corteva?

We welcome all efforts to provide farmers with more choices and information. Our own vision is to use CRISPR to develop a variety of crops with added environmental and consumer benefits. Over time, we believe these benefits will create broad acceptance for CRISPR-produced seeds among producers and consumers alike.

#### Will Corteva create CRISPR-produced plants with direct consumer benefits?

Consumers are demanding food that is healthier for them and is grown with less environmental impact. We need to keep developing technologies to meet these goals. CRISPR is one tool that can help.

We continue to research and develop seed products with CRISPR technology and have product concepts underway with direct consumer benefits such as healthier oil.





## Social License and Public Acceptance

## Why are you bringing these products to market? Do consumers even want CRISPR products?

Consumers are demanding food that is healthier for them and the environment. Examples of potential benefits that consumers are interested in include crops that taste better and have more vitamins and nutrients, food that is less expensive due to the use of fewer resources to grow crops, and less food waste due to fruits and vegetables that don't brown or rot quickly. We need to keep developing products to meet these goals. CRISPR is one tool that can help.

# Do you feel it is your role to educate the public about CRISPR? How will you share information about CRISPR-produced plants with the public?

Corteva Agriscience™ is proud of our exploration of plant breeding innovations such as CRISPR to produce healthier, more nutritious and sustainable crops, and we are committed to transparency and making information about CRISPR available to our partners and consumers.

Here are some examples of our transparency and engagement around CRISPR:

- Through our Insight Series, we have engaged and listened to stakeholders with diverse viewpoints to help us better understand perspectives about technology and food.
- We support international forums, such as CRISPRCon, that give voice to people whose lives could be impacted by this breakthrough technology.
- We continue to engage and seek feedback from stakeholders who will play a critical role in assessing the potential of CRISPR to make the transition from the lab to the family table.

# Do you think CRISPR will face the same public scrutiny as GMOs? Do you think consumers will ultimately accept CRISPR?

Consumers are demanding healthier food grown with less environmental impact. If they understand that CRISPR is a tool that works within the genetic material already existing in the plant to achieve these goals safely and efficiently, we believe the public will enthusiastically adopt CRISPR-produced plants.

Almost any new technology prompts questions and hesitation. That's appropriate and to be expected. A large part of our role as users of this technology is to address those questions and concerns using fact-based, scientific information, and to explain the benefits of products developed with CRISPR in the practice of sustainable agriculture. We plan to do our part to educate and inform all our stakeholders as we move forward with the use of this technology.





We fully believe consumers will embrace and benefit from CRISPR – it's part of why we are so excited to invest in this area of our business.

## How can the public be sure Corteva Agriscience™ will use CRISPR responsibly?

We are deeply committed to putting our customers and their needs first, and to ensuring that every product we provide is made responsibly. At Corteva, we've developed a set of guiding principles for our applications of CRISPR as an advanced plant breeding tool. Examples of those principles include:

- Corteva products developed using CRISPR for advanced plant breeding include only genetic material from the target plant/crop.
- Corteva is committed to open, transparent and timely communications about its use of CRISPR.
- Corteva supports appropriate, science-based regulatory oversight for plants developed with CRISPR, consistent with those for plants developed through other plant breeding methods.

Corteva extensively field-tests all new varieties we develop to confirm changes were made as intended. Specifically, for CRISPR-produced plants:

- Corteva researchers confirm the intended change was successful.
- Corteva researchers conduct field tests of thousands of plants over several years to confirm that plants grow and perform as intended.
- Corteva engages routinely with regulatory agencies like the FDA about our products. We adhere to all FDA food safety regulations for all our products.

#### **Open Innovation and Intellectual Property**

## Does Corteva have its own IP for the CRISPR technology?

Yes. In addition to licensed intellectual property rights from the Broad Institute of MIT and Harvard, the University of California, Berkeley (through alliances with Caribou Biosciences and ERS Genomics) and Vilnius University, the Corteva (DuPont and Pioneer Hi-Bred) patent portfolio comprises patent applications related to the CRISPR technology.

## What is Corteva's licensing agreement with the Broad Institute?

Corteva has received non-exclusive global rights to the Broad Institute patent portfolio covering intellectual property for CRISPR-Cas9 gene-editing technology for all agricultural uses and applications.

What are the terms of the licensing agreement? How much was invested?





We are not disclosing the specific terms or financial details of the licensing agreement. What we can share is that Corteva Agriscience<sup>TM</sup> maintains a substantial commitment to CRISPR technology for agricultural applications.

## Will you sub-license your access to Broad Institute Technology?

Corteva and the Broad Institute have entered an alliance through which they are committed to jointly enable others in the plant agriculture field with comprehensive licenses to their joint CRISPR-Cas9 intellectual property portfolio. Corteva (previously DuPont Pioneer) has a long history of collaboration and a commitment to broadly advancing science. Corteva is collaborating to develop the technology across all crops and geographies for the greater good. (Examples include: CIMMYT, Danforth Center.)

We have secured non-exclusive rights to the Broad IP under which we can out-license traits and products made using CRISPR-Cas9 technology. Should an entity want to license only the Broad IP, they can contact Broad Institute directly; if an entity desires a license to Pioneer IP only, we are happy to provide such a license. Most frequently, however, interested parties take a license under Corteva and the Broad Institute's joint licensing program.

# Is there any entity that would not qualify for license agreements through the Corteva (DuPont) and Broad joint licensing agreement?

The scope of the joint licensing framework for agriculture covers plant applications, subject to certain restrictions. Animal or human therapeutic applications are not included under the joint licensing framework.

#### Are there any agricultural applications that would be prohibited use under the joint licensing agreements?

Yes: gene drives, commercial tobacco products for human use, and sterile seed engineering that prevents replanting (terminator seed) are applications that are prohibited under the joint licensing framework.

## What applications are covered under Corteva's non-exclusive licensing agreement?

All agricultural applications in plants, plant cells and organs, including row crops, fruits, vegetables, nuts, grasses, trees and agricultural biologicals.

How does the licensing agreement with the Broad Institute differ from your current exclusive licenses with ERS Genomics, Caribou Biosciences and Vilnius?





This licensing agreement is in addition to the licensing agreements that we have previously announced with ERS Genomics, Caribou Biosciences and Vilnius University and provides Corteva with a comprehensive set of foundational CRISPR-Cas9 IP.

# Isn't this just a way for Corteva Agriscience<sup>TM</sup> and the Broad Institute to unfairly control access to CRISPR technology?

Just the opposite, in fact. The goal of developing a joint licensing framework is to provide democratic access to CRISPR-Cas9 for agricultural applications in plants. We intend to enable third parties so that the abundant potential of CRISPR can be better realized. Corteva has and will continue to enable others by providing access to its CRISPR technology.

## What are the licensing terms for third parties under the joint licensing framework between Corteva and the Broad Institute?

We are not publicly disclosing terms of the joint licensing framework. All parties interested in obtaining a license are invited enter a three-way confidentiality agreement with Pioneer and the Broad Institute under which the terms can be disclosed to bona fide potential licensees. Generally speaking, the financial terms of the joint license are adapted to the R&D resources of the potential licensees, to provide reasonable terms that encourage adoption of CRISPR technology to further advancements in agriculture. Free licenses are being made available to universities and nonprofit organizations for academic research and to nonprofit organizations developing products for smallholder farmers.

#### What is Open Innovation and what does Corteva intend to accomplish?

Through our Open Innovation initiative, Corteva collaborates with thought leaders and innovators to identify and develop solutions to some of the world's most pressing food and agriculture needs. Our Open Innovation platform creates a mechanism to rapidly deploy innovative technologies through organizations that are good stewards of those technologies. This approach enables the development of tailored solutions to address local problems around the world.

We're calling on small and large companies, public research institutes and academia to come together to drive innovation that will enable us to solve the pressing challenges facing us in agriculture.

Corteva has an Open Innovation program in traits, plant breeding, enabling technologies, biologicals, crop protection and digital solutions. For more information, go to <a href="https://www.openinnovation.corteva.com">www.openinnovation.corteva.com</a>.

#### What are the terms for Corteva's Open Innovation partners?





Terms for Open Innovation projects are tailored on a case-by-case basis. They are generally structured to encourage the easy implementation of small-scale collaborations with non-controversial intellectual property and data ownership terms.

## Can you share some examples of Corteva Agriscience™ CRISPR Open Innovation partnerships?

In September 2016, DuPont Pioneer and the International Maize and Wheat Improvement Center (CIMMYT) announced a public/private partnership to jointly develop improved crops using CRISPR to address the needs of smallholder farmers around the world.

The Pioneer-CIMMYT Steering Committee is currently considering a range of potential products and target traits. The first project applies CRISPR to address the devastating maize lethal necrosis (MLN) disease in sub-Saharan Africa.

The International Crops Research Institute for the Semi-Arid Tropics (ICRISAT) and Corteva also inked a multiyear partnership to strengthen food security by improving crops that feed millions through sharing of high-tech and modern breeding technologies.

Corteva and the Donald Danforth Plant Science Center entered a collaboration to apply cutting-edge technologies, including CRISPR and Pioneer Hi-Bred's proprietary developmental genes technology, for creating new varieties of improved food security crops with enhanced native traits.

#### **Human Medicine**

#### How can CRISPR be used in human medicine?

Researchers are using CRISPR to discover treatments and cures for serious genetic diseases and conditions, such as certain types of cancer, sickle cell anemia, cystic fibrosis and early-onset Alzheimer's. These innovations and advancements, made possible through CRISPR, have the potential to improve the lives of millions.

What is the stance of Corteva on the Chinese scientist who used CRISPR to edit embryos, resulting in the live birth of gene edited twins?

Corteva is not involved in human medical research. Our research is in agriculture and our work with CRISPR is focused specifically on growing healthy and nutritious crops. We are committed to being open and transparent about our use of CRISPR to improve agriculture and food.

What about those studies raising questions about unintended consequences in human medicine?





Corteva Agriscience<sup>TM</sup> is not involved in human medical research, a use of CRISPR completely outside the scope of our own application of the technology. We will note, however, that any study needs to be assessed based on the principles of peer-reviewed science.