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Building 600/700, Suite 7-501
Cambridge, MA 02139



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February 12, 2024
Bernadette Juarez
APHIS Deputy Administrator
Biotechnology Regulatory Services

RECEIVED

By ajdrummond for BRS Document Control Officer at 9:55 am, Feb 13, 2024

Sent electronically to RSRrequests@usda.gov

Contains Confidential Business Information

Re: Request for a Regulatory Status Review under 7 CFR part 340 of gene edited maize lines with increased yield

Dear Ms. Juarez,

Inari Agriculture, Inc. (Inari) uses genetic technologies and data science to develop next-generation seeds that reduce the natural resources required to grow our food, while providing farmers with more choice, performance, and value.

Inari is developing and intends to potentially commercialize maize (*Zea mays* L.) lines with increased yield through modified plant architecture that have been edited using a Cas enzyme system. Planned activities include, but would not be limited to, seed and grain production that would require import, interstate movement, and unconfined environmental release. Inari respectfully requests a Regulatory Status Review from the USDA APHIS Biotechnology Regulatory Service (BRS), of the maize lines.

For your evaluation, the attached appendix includes the information requested in the "Guide for Requesting a Regulatory Status Review under 7 CFR part 340" (Document BRS-GD-2020-0003).

This Regulatory Status Review request contains CBI. We are protecting the following as CBI within our submission:

- Details of the line phenotype and mode of action resulting from the intended gene modifications discussed
- Gene names, protein names, and their function
- Select details of genome modifications
- Select details of methodology and processes
- Any literature relating to the above-referenced information

The above-referenced information will reveal commercially valuable details on our product concepts and portfolio. Information claimed as CBI is customarily kept private or closely held, in the context of




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industry practices concerning the information. The release of this information will cause significant financial harm to Inari by making such information available to our competitors and reveal our business and technical strategy. The current technical space in which we operate is highly competitive and any release of information would undermine the current and future success of Inari's business. Furthermore, the above-referenced information has not yet been patented and any disclosure would impact novelty and impact the validity of any future patent filings on this material and processes. Where commercial or financial information is both customarily and actually treated as private by its owner and provided to the government under an assurance of privacy, the information is "confidential" within the meaning of 5 U. S. C. §552(b)(4), the Freedom of Information Act's Exemption 4.

We thank the USDA APHIS BRS in advance for your consideration of this request and we welcome any questions you may have about our inquiry.

Sincerely,

DocuSigned by:

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Rachel Gast

Senior Director, Regulatory

Inari Agriculture, Inc.

rgast@inari.com

774-233-8594



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Request for a Regulatory Status Review (RSR) under 7 CFR part 340, of gene edited maize lines with enhanced yield characteristics

Confidential Appendix

1. Information about Requestor

Requestor/Developer

Inari Agriculture, Inc.
One Kendall Square
Building 600/700, Suite 7-501
Cambridge, MA 02139

Contact:

Rachel Gast; Senior Director, Regulatory
rgast@inari.com
Ph: 774-233-8594

2. Confidential Business Information (CBI) Statement

This RSR Request contains CBI.

Justification Statement:

We are protecting the following as CBI within our submission:

- Details of the line phenotype and mode of action resulting from the intended gene modifications discussed
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the government under an assurance of privacy, the information is “confidential” within the meaning of 5 U. S. C. §552(b)(4), the Freedom of Information Act’s Exemption 4.

3. Description of Comparator Plant (*Zea mays* L.)

The comparator plant for the modified maize lines described here, is any variety of *Zea mays* L. produced through conventional breeding.

The classification of maize, according to the PLANTS Database of the USDA Natural Resources Conservation Service: Plant Database (USDA NRCS, 2022), is as follows:

Taxonomic Rank	Name
Order	Cyperales
Family	Poaceae
Genus	<i>Zea</i> L.
Species	<i>Zea mays</i> L.

The biology of maize is described in detail by OECD in the “Consensus document on the biology of *Zea mays* subsp. *mays* (maize)” (OECD, 2003).

Maize does not possess weediness, invasiveness, or dormancy characteristics and is not listed as a noxious weed pursuant to 7 CFR Part 360. Maize is unable to survive in the wild due to its long process of domestication and requires human intervention to disseminate its seed. It is possible for maize from commercial plantings to overwinter and germinate the following year, but it cannot persist as a weed and is easily controlled mechanically or chemically. Maize is therefore incapable of sustained reproduction outside of domestic cultivation and is non-invasive in natural habitats (OECD, 2003).

USDA APHIS BRS has reviewed the potential weediness of maize in response to several petitions for deregulation of genetically modified maize varieties. Cited literature in these assessments supports the conclusion that maize does not possess weediness characteristics.

4. Genotype of the Modified Plant (No DNA Inserted)

A. Name of the altered genetic component and nature of modification(s):

Name of the Altered Genetic Component

The maize lines were modified using a Cas enzyme and native repair mechanism in the [] of the [] maize endogenous gene to

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enhance yield (Phenotype and mechanism of action further described in **Section 5**). []

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Nature of the Modification

There is no inserted DNA in the final maize lines, as an endogenous maize gene promoter was modified to create the lines and the Cas enzyme and guide RNAs introduced for editing are segregated away from the final line through selection and breeding steps.

The maize lines have a type of [] which is used to modify the function of the selected genes. [] is achieved by creating []

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[] will occur as a result of normal DNA repair mechanisms and without the use of a template. This type of edit falls into the classification often referred to as site directed nuclease type 1, or SDN-1. The resultant modifications create changes to the [] sequence that are similar to what would be expected through conventional breeding. The [] modifications are intended to []. There will be no sequence modifications in the [] the gene. In the maize lines described here, [] double-strand breaks were made to create a [] deletion in the []

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B. Sequence of the Modification:

FASTA Sequences of the modified lines are provided in Figures 1-3 below []

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C. Sequence Comparison

The [] sequence of the [] gene has been previously published and described in maize variety []. This gene is also present in other maize variety backgrounds. [] of the [] gene have been previously described in []. The area highlighted in Figure 4 is the location of one of these deletions []. Inari [] edited lines [] have a comparable deletion in the [] region as shown in the sequence comparison (Figure 4). As may be seen in Figure 4, the size of the edit can vary between the edited lines. However, although this may be the case, we would anticipate that if additional modified plants are created in the future with comparable edits, they would express functionally equivalent modifications to those described in this application.

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5. Description of New Trait

A. Intended Trait

The intended trait is an enhancement in yield.

B. Intended Phenotype

Based on the information in [] the intended phenotype of the [] edited lines is anticipated to be an increase in yield related traits such as increased size and number of reproductive organs [].

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C. Description of the Mechanism of Action (MOA)

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]. Edits [
] of a signaling component gene involved in meristem regulation may lead to an increase in yield related traits such as increased size and number of reproductive organs.

References:

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OECD (2003) Consensus Document on the Biology of *Zea mays* subsp. *mays* (Maize). Series on Harmonisation of Regulatory Oversight in Biotechnology, No. 27, OECD Publishing, Paris. <http://www.oecd.org/env/ehs/biotrack/46815758.pdf> (accessed 8 June 2020)

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USDA, NRCS. 2020. The PLANTS Database (<http://plants.usda.gov>, 14 November, 2022). National Plant Data Team, Greensboro, NC 27401-4901 USA