CONFIDENTIAL

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

CBI-Del Copy

November 8, 2023
Bernadette Juarez
APHIS Deputy Administrator
Biotechnology Regulatory Services

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 modified plant architecture

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 modified plant architecture that have been edited using a proprietary 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 revised 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

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.

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:
Sarah Forrester
8861830DF5644AF...

Sarah Forrester

Director, Regulatory

Inari Agriculture, Inc.

sforrester@inari.com

Ph: 774-233-8594

Request for a Regulatory Status Review (RSR) under 7 CFR part 340, of gene edited maize lines with modified plant height

Confidential Appendix

1. Information about Requestor

Requestor/Developer

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

Contact:
Sarah Forrester, Director Regulatory
sforrester@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
- 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. 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.

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 (2022), is as follows:

Taxonomic rank	**Name**
Order	Cyperales
Family	Poaceae
Genus	*Zea* L.
Species	*Zea mays* L.

4. Genotype of the Modified Plant (Genetic Material is Inserted)

Inari is developing maize lines with modifications in plant architecture with an objective to modify plant height and has identified a [ ], in the maize genome that **CBI-Del**
bears strong similarity to a known transcription enhancer element, a sequence that also occurs in the
genomes of other crops such as [ ]. Insertion of this small native maize enhancer **CBI-Del**
element leads to reliable upregulation of a [**CBI-Del**
CBI-Del
]. **CBI-Del**

[ ] of the native enhancer element would be inserted, using an efficient CRISPR/Cas- **CBI-Del**
mediated DNA insertion technology, at a specific location into the native maize promoter of [ ] **CBI-Del**
during non-homologous end joining (NHEJ)-mediated repair of CRISPR/Cas-induced double-stranded
breaks. The modification results in [ ]. **CBI-Del**

Only the native maize transcription enhancer element remains in the final product as the vector
sequence (including the [ ] introduced for editing) is segregated away from **CBI-Del**
the final line through selection and breeding steps.

A. Sequence of the insertion:

FASTA nucleotide sequences of the examples of the inserted genetic material remaining in the modified lines are provided below representing examples of [**CBI-Del**

CBI-Del
CBI-Del

CBI-Del
CBI-Del

CBI-Del
CBI-Del

CBI-Del
CBI-Del

CBI-Del
] **CBI-Del**

B. Annotation of the Inserted Genetic Material

Only the native maize transcription enhancer element remains in the final product. Depending on the design, maize lines will include [**CBI-Del**
]. In addition, **CBI-Del**
insertion of the enhancer element may result in small deletions around the insertion site.

C. Genetic Components

Nucleotide Position	**Name of Inserted Component**	**Construct Component Donor**	**Function**
[ ]	Transcription enhancer element	*Zea mays* L.	Insertion of this small maize enhancer element leads to reliable upregulation of a [ ].

CBI-Del
CBI-Del
CBI-Del

In Figure 1, the highlighted blue sequence indicates the intended region for insertion where the first base pair is the beginning of [ ] in the maize genome. The yellow indicates the start of the [ ] gene coding sequence. **CBI-Del**
CBI-Del

CBI-Del Copy

[**CBI-Del**

CBI-Del

] **CBI-Del**

5. Description of New Trait

A. Intended Trait

The intended trait is a modification in plant height.

B. Intended Phenotype

The insertion of the maize enhancer in the promoter of [ ] increases the expression of the **CBI-Del**
[**CBI-Del**
CBI-Del
]. **CBI-Del**

C. Description of the Mechanism of Action (MOA)

The [ ] gene encodes the maize [**CBI-Del**
CBI-Del
]. These two studies showed that natural variation in the expression level of **CBI-Del**

CBI-Del Copy

[**CBI-Del**
CBI-Del
CBI-Del
]. **CBI-Del**

[**CBI-Del**
]. Insertion of the small native maize enhancer **CBI-Del**
element in the [ ] in maize results in a modified response to gibberellin **CBI-Del**
hormones.

[**CBI-Del**
CBI-Del
CBI-Del
CBI-Del
CBI-Del
CBI-Del
CBI-Del

CBI-Del
CBI-Del
CBI-Del
CBI-Del
]. **CBI-Del**

References:

[**CBI-Del**
CBI-Del
] **CBI-Del**

[**CBI-Del**
] **CBI-Del**

[**CBI-Del**
CBI-Del
CBI-Del
] **CBI-Del**

[**CBI-Del**
] **CBI-Del**

CBI-Del Copy

[**CBI-Del**
] **CBI-Del**

[**CBI-Del**
CBI-Del
CBI-Del
CBI-Del
] **CBI-Del**

Organization for Economic Co-operation and Development (2003). Consensus document on the biology of zea mays subsp. mays (maize). **http://www.oecd.org/env/ehs/biotrack/46815758.pdf**

United States Department of Agriculture, Natural Resources Conservation Service (2022). The PLANTS Database. **http://plants.usda.gov**