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

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April 26, 2024
Bernadette Juarez
APHIS Deputy Administrator
Biotechnology Regulatory Services

RECEIVED*By kldiggs for BRS Document Control Officer at 9:02 am, Apr 29, 2024*

Sent electronically to RSRrequests@usda.gov

Contains Confidential Business Information (CBI)

**Re: Request for a Regulatory Status Review (RSR) under 7 CFR part 340 of gene edited soybean lines
with enhanced yield characteristics**

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 soybean (*Glycine max* (L.) Merr.) lines with enhanced yield characteristics 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 soybean 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 I 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



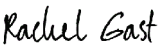
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above-referenced information has not yet been patented and any disclosure would impact novelty and impact the validity of any future patent filings on this material and processes. Where commercial or financial information is both customarily and actually 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:

D8A4AC00810F4AD...
Rachel Gast

Senior Director, Regulatory

Inari Agriculture, Inc.

rgast@inari.com

774-223-8594



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Request for a Regulatory Status Review (RSR) under 7 CFR part 340 of gene edited soybean 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
774-233-8594

2. Confidential Business Information Statement

This RSR Request contains CBI-Del.

Justification Statement

We are protecting the following as CBI-Del 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-Del 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. 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.



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3. Descriptor of Comparator Plant (*Glycine max* (L.) Merr.)

The comparator plant for the modified soybean lines described here, is any variety of *Glycine max* (L.) Merr. produced through conventional breeding.

The classification of soybean, according to the PLANTS Database of the USDA Natural Resources Conservation Service: Plant Database (USDA NRCS, 2023), is as follows:

Taxonomic Rank	Name
Order	Fabales
Family	Fabaceae Lindl.
Genus	<i>Glycine</i> Willd.
Species	<i>Glycine max</i> (L.) Merr.

4. Genotype of the Modified Plant (No genetic material Inserted)

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

Name of the Altered Genetic Component

Inari is developing soybean lines with modifications in plant architecture through [] of one or more specific endogenous gene targets. [] of these gene targets creates genome modifications and phenotypic variation of the kind that can be expected to occur through conventional breeding practices, as no new or interspecific sequences are introduced. The resulting modifications in soybean plant architecture traits are intended to increase yield.

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Inari has selected several gene targets that modify plant architecture. The soybean gene targets include [

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In developing lines, Inari is modifying these selected genes individually or in varying combinations of [] genes to achieve the desired phenotype. Soybean lines containing the [] edited gene targets [] have previously been assessed as part of an ‘Am I regulated’ application and the USDA concluded that the genome edited lines were not regulated pursuant to 7 CFR part 340 (Juarez, 2020). The purpose of this application is to request an assessment of edited lines which may also contain modification to the []. For completeness, the information in this submission covers all [] genes and the RSR request extends to lines that have already been produced [] as well as lines that Inari intends to produce [].

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Nature of the Modification

There is no inserted DNA in the final soybean lines, as endogenous [] are modified to create the lines. The Cas enzyme and guide RNAs introduced for editing are segregated away from the final line through selection and breeding steps.

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[] are achieved by creating a targeted double-strand break in the gene region. This results in deletions of variable size at the break site that [].

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[] is achieved by creating one or more targeted double-strand breaks in the target gene []. The breaks are created through one or more guides in the editing construct. This results in [

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insertions, or inversions of variable size and structure at locations including, but not limited to, the binding sites for activating transcription factors. These DNA modifications [10], thereby influencing plant phenotype characteristics as controlled by the endogenous gene. There are no [11] from the gene.

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The edits are created through the use of a CRISPR-Cas gene editing system which generates double-strand breaks in the DNA of each targeted sequence which are then repaired by normal DNA repair mechanisms without the use of a template.

B. Sequence of the Modification

FASTA Sequences of the modified lines are provided in Figures 1-12 below. For each figure the gene [] is included as the edited region for [].

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C. Sequence Comparison

Comparisons of the wild type sequences with the edited sequences for [] lines containing [] may be seen in Figures 13-24 below. Although specifics like the size of the edit for each gene can vary between edited lines, we anticipate that if additional modified plants are created in the future, they would be functionally equivalent to those described in this application.

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D. Reference Numbers:

Gene Name	Accession Number Wm82.a2.v1 /Glyma2.0
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5. Description of New Trait

A. Intended Trait

The intended trait is an enhancement in yield.

B. Intended Phenotype

The sequence edits render changes to the function of these genes leading to changes in certain agronomic yield characteristics such as [].

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C. Description of the Mechanism of Action (MOA)

This application is a request for a regulatory status review of soybean lines which contains edits to targeted genes in soybean. As described above, soybean lines containing [] of the edited gene targets have previously been assessed as part of an ‘Am I Regulated’ application and the USDA concluded that the genome edited lines were not regulated pursuant to 7 CFR part 340 (August 6, 2020). The purpose of this application is to request an assessment of edited lines containing the additional [] gene.

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In developing lines, Inari is modifying these identified genes individually or in varying combinations of [] genes to achieve the desired phenotype. A description of each of the targeted genes is provided below. In sum, Inari is modifying [] to alter the reproductive transition timing by creating a [] loss of protein expression of one or more of these genes involved in regulating the transition between vegetative and reproductive growth. Inari is modifying [] to increase seed size by decreasing production of a suppressor of cell division and Inari is modifying [] to increase seed number by modifying cell division.

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Juarez, B. (2020). Confirmation of the regulatory status of genome edited soybean lines. USDA APHIS BRS
[https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/Regulated Article Letters of Inquiry](https://www.aphis.usda.gov/aphis/ourfocus/biotechnology/Regulated%20Article%20Letters%20of%20Inquiry)

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Organisation for Economic Co-operation and Development (2000). Consensus document on the biology of
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United States Department of Agriculture, Natural Resources Conservation Service (2023). The PLANTS
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