Date of Approval: December 10, 2018

FREEDOM OF INFORMATION SUMMARY

SUPPLEMENTAL NEW ANIMAL DRUG APPLICATION

NADA 141-454

AquAdvantage Salmon

opAFP-GHc2 rDNA construct in EO-1α lineage Atlantic salmon

The effect of the supplemental approval is to update the analytical method (polymerase chain reaction or PCR) to identify AquAdvantage Salmon.

Sponsored by:

AquaBounty Technologies, Inc.

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I. GENERAL INFORMATION

A. File Number

NADA 141-454

B. Sponsor

AquaBounty Technologies, Inc.
Two Clock Tower Place, Suite 395
Maynard, MA 01754

Drug Labeler Code: 086053

C. Proprietary Name

"AquAdvantage Salmon", *opAFP-GHc2* rDNA construct in the EO-1α lineage of Atlantic salmon

D. Species/Class

Atlantic salmon

E. Indication

Significantly more AquAdvantage Salmon grow to at least 100 g within 2,700 ^{0}C-days than their comparators.

F. Effect of Supplement

To update the analytical method (polymerase chain reaction or PCR) to identify AquAdvantage Salmon.

II. PRODUCT DEFINITION

This supplemental approval does not change the previously approved Product Definition. The Freedom of Information (FOI) Summary for the original approval of NADA 141-454 dated November 19, 2015, contains the Product Definition.

The product definition for the approved application is:

Product Identity

A single copy of the a-form of the opAFP-GHc2 rDNA construct at the a-locus in the EO-1a lineage triploid, hemizygous, all-female Atlantic salmon (Salmo salar) known as AquAdvantage Salmon.

Claim
Significantly more AquAdvantage Salmon grow to at least 100 g within 2,700 ^{0}C-days than their comparators.

Limitations for Use
AquAdvantage Salmon are produced as eyed-eggs and grown-out only in physically-contained freshwater culture facilities specified in an FDA-approved application.

III. MOLECULAR CHARACTERIZATION OF THE CONSTRUCT

CVM did not require additional studies and information related to this technical section for this supplemental approval. The FOI Summary for the original approval of NADA 141-454 dated November 19, 2015, contains a summary of all information for "Molecular Characterization of the Construct." That information remains valid.

IV. MOLECULAR CHARACTERIZATION OF THE GE ANIMAL LINEAGE

CVM did not require additional studies and information related to this technical section for this supplemental approval. The FOI Summary for the original approval of NADA 141-454 dated November 19, 2015, contains a summary of all information for "Molecular Characterization of the GE Animal Lineage." That information remains valid.

V. PHENOTYPIC CHARACTERIZATION OF THE GE ANIMAL

CVM did not require additional studies and information related to this technical section for this supplemental approval. The FOI Summary for the original approval of NADA 141-454 dated November 19, 2015, contains a summary of all information for "Phenotypic Characterization." That information remains valid.

VI. GENOTYPIC AND PHENOTYPIC DURABILITY

CVM did not require additional studies and information related to this technical section for this supplemental approval. The FOI Summary for the original approval of NADA 141-454 dated November 19, 2015, contains a summary of studies for "Genotypic and Phenotypic Durability." Those studies and information remain valid.

VII. HUMAN FOOD SAFETY

A. Food Safety

CVM did not require additional information to assess food consumption risks for this supplemental approval. The FOI Summary for the original approval of NADA 141-454 dated November 19, 2015, contains a summary of all studies and information used to assess food safety. Those studies and information remain valid.

B. Analytical Method

The sponsor provided an updated analytical method of identity from the method described in Appendix 3 of the FOI Summary for the original approval of NADA 141-454 dated November 19, 2015, and is described below.

AquAdvantageSalmon have an enhanced growth phenotype when compared to farm-raised non-genetically engineered (non-GE) Atlantic salmon that allows them to grow faster. However, at market size, the AquAdvantageSalmon are not phenotypically distinguishable from non-GE farm-raised Atlantic salmon. The FDA requires that animals of species that are traditionally consumed as food must have an analytical method designed to detect the presence of the opAFP-GHc2 construct in tissues or edible products from these GE animals.

An updated multiplex polymerase chain reaction (PCR) procedure used by the sponsor to confirm both the genotype of the AquAdvantage Salmon and the location of the integration site for the opAFP-GHc2 construct at the α- locus was provided to FDA. The updated method provides new PCR primers to improve specificity and interpretation of the results. This is the method the sponsor proposes to use for routine genotyping and surveillance of product durability and hence it is their proposed analytical method for monitoring.

The analytical method is capable of discriminating between the AquAdvantage Salmon and their non-GE counterparts. The sponsor's proposed PCR assay uses three multiplex PCR reactions. Each reaction uses a primer pair for the endogenous salmon cyclin gene as a control for successful PCR amplification from a salmon sample. Each reaction also contains another primer pair that is specific to a different region of the opAFP locus. The primer pairs detect the 5' junction with the salmon genome, the 3' junction with the salmon genome, and the growth hormone region of the insert. Because the primers at the 5' and 3' junctions span the junction of the insert into the genome, they confirm that the fish is an AquAdvantage Salmon containing the opAFP-GHc2 construct at the α-locus.

In addition to being able to distinguish AquAdvantage Salmon from non-GE salmon in a mixed population, this method also is capable of (1) identifying muscle tissue from AquAdvantage® Salmon, (2) identifying a durability failure, and (3) discriminating between the AquAdvantage® Salmon and a knock-off (other GE fish containing similar constructs that are not AquAdvantage® Salmon).

We conclude that this method is suitable for the purposes proposed by the sponsor and is capable of determining genotype and confirming rDNA integration at the described α- locus. Further, the method has been validated at CVM's Office

of Research laboratory. This validated PCR method meets the agency's requirements for a practicable method to identify the presence of the opAFP-GHc2 construct in fish. The method replaces the original method described in the November 19, 2015, original approval. The method is on file at the Center for Veterinary Medicine, 7500 Standish Place, Rockville, MD 20855. To obtain a copy of the analytical method, please submit a Freedom of Information Summary request to: https://www.accessdata.fda.gov/scripts/foi/FOIRequest/requestinfo.cfm.

VIII. EFFECTIVENESS/CLAIM VALIDATION

CVM did not require additional effectiveness/claim validation studies and information for this supplemental approval. The FOI Summary for the original approval of NADA 141-454 dated November 19, 2015, contains a summary of studies for "Effectiveness/Claim Validation." These studies remain valid.

IX. AGENCY CONCLUSIONS

FDA concludes that the data submitted in support of this supplemental NADA satisfy the requirements of section 512 of the Federal Food, Drug, and Cosmetic Act and 21 CFR Part 514. The data subject to the current supplement demonstrated that the analytical method of identity is suitable for determining genotype and confirming rDNA integration at the described intended locus in the genome. All other NADA requirements are satisfied in the original and supplemental approvals of NADA 141-454 dated November 19, 2015, and April 26, 2018.

A. Supplemental Application

This supplemental NADA did not require a reevaluation of the safety or effectiveness data in the original NADA (21 CFR 514.106(b)(1).

B. Patent Information:

For current information on patents, see the Animal Drugs @ FDA database or the Green Book on the FDA CVM internet website.