Hogan Lovells US LLP
Columbia Square
555 Thirteenth Street, NW
Washington, DC 20004
T +1 202 637 5600
F +1 202 637 5910
www.hoganlovells.com

MEMORANDUM

From: Martin J. Hahn
Veronica Colas
Leigh G. Barcham

Date: July 6, 2020

Re: AMS Issues Final Guidance on Detectability Testing and Validation of Refining Processes Under the National Bioengineered Food Disclosure Standard

The U.S. Department of Agriculture's (USDA's) Agricultural Marketing Service (AMS) issued two final guidance documents providing industry stakeholders with instructions on how to implement certain requirements of the National Bioengineered Food Disclosure Standard (NBFDS). The agency's Guidance to Ensure Acceptable Validation of a Refining Process outlines steps for validating that a refining process makes modified genetic material undetectable in a food. 1/ AMS's Guidance on Testing Methods provides considerations for the selection of a test method to ascertain that a food or ingredient does not contain detectable modified genetic material and therefore does not require a bioengineered food disclosure. 2/ AMS issued draft versions of the guidance documents in December 2019 3/ and February 2020 4/, respectively. AMS also issued new Frequently Asked Questions (FAQs) corresponding to each of the guidance documents. This memorandum summarizes the guidance documents and FAQs, but we encourage any entity relying on the use of a validated refining process or testing to establish that a food is not subject to disclosure under the NBFDS to read the documents in their entirety.

1/ Guidance to Ensure Acceptable Validation of a Refining Process, available at https://www.ams.usda.gov/sites/default/files/media/NBFDS_ValidationGuidance.pdf; *see also* Frequently Asked Questions: Guidance to Ensure Acceptable Validation of a Refining Process, available at https://www.ams.usda.gov/sites/default/files/media/NBFDS_FAQrefiningProcessValidation.pdf.

2/ National Bioengineered Food Disclosure Guidance on Testing Methods, available at https://www.ams.usda.gov/sites/default/files/media/NBFDS_testingMethodology.pdf; *see also* Frequently Asked Questions: Guidance on Testing Methods, available at https://www.ams.usda.gov/sites/default/files/media/NBFDS_FAQtestingMethods.pdf.

3/ *See* AMS Releases Draft Instructions on Validating a Refining Process for National Bioengineered Food Disclosure Standard (Jan. 7, 2020), available at https://www.hlfoodlaw.com/2020/01/ams-releases-draft-instructions-on-validating-a-refining-process-for-national-bioengineered-food-disclosure-standard/.

4/ *See* AMS Releases Draft Instructions on Testing Methods for the National Bioengineered Food Disclosure Standard (Feb. 6, 2020), available at https://www.hlfoodlaw.com/2020/02/ams-releases-draft-instructions-on-testing-methods-for-the-national-bioengineered-food-disclosure-standard/.

Background

On July 29, 2016, Congress established the National Bioengineered Food Disclosure Act, establishing a national standard for disclosing that a food is or may be bioengineered. In its regulations implementing the new law, AMS defined a "bioengineered food" as "A food that contains genetic material that has been modified through in vitro recombinant deoxyribonucleic acid (rDNA) techniques and for which the modification could not otherwise be obtained through conventional breeding or found in nature; *Provided that such a food does not contain modified genetic material if the genetic material is not detectable pursuant to § 66.9*" (emphasis added). In other words, a food is not a bioengineered food and does not require a bioengineered food disclosure if it does not contain detectable modified genetic material.

In § 66.9(a) of its implementing regulations, AMS established three ways to show modified genetic material is not detectable:

1. Records to verify that the food is sourced from a non-bioengineered crop or source;

2. Records to verify that the food has been subjected to a refinement process validated to make the modified genetic material in the food undetectable; and

3. Certificates of analysis or other records of testing appropriate to the specific food that confirm the absence of modified genetic material.

The guidance documents provide clarity on validating refinement processes under § 66.9(a)(2) and testing to confirm the absence of modified genetic material under § 66.9(a)(3).

Validation of Refining Processes

The Guidance to Ensure Acceptable Validation of a Refining Process lays out steps for validating that a refining process will remove detectable modified genetic material. The steps are similar to those included in the draft version of the guidance, though AMS uses terminology that is less closely associated with food safety programs (e.g., "critical control point" or CCP). The steps are as follows:

1. **Identify raw materials, ingredients, and product- contact materials.**

2. **Define characteristics and intended end use of the product (for these purposes, the defining characteristic would be that modified genetic material is undetectable).**

3. **Define the sequence and interaction of all processing steps used to arrive at the end product.**

4. **Identify the key step or steps in the refinement process that may influence the end product's characteristics and its ability to meet specified requirements.** In other words, determine the step that renders modified genetic material undetectable or the series of steps after which modified genetic material is undetectable. The series of steps may include the entire process. Define the measurable parameters (i.e., time, temperature, content level) and decision criteria (i.e., limits) that make a step a key step.

5. **Assemble relevant validation information that demonstrates the refinement process operates as intended to meet specific requirements (end product characteristics), conducting studies as needed**. AMS explains that the collection of evidence/data to demonstrate that a key step(s) consistently and effectively makes modified genetic material undetectable can be achieved through a variety of approaches. Where other data sources do not exist, testing is often a means to collect evidence and demonstrate modified genetic material is undetectable. When testing is conducted in this circumstance, AMS clarifies it is performed once as part of the validation process and is separate from ongoing end-product testing performed under § 66.9(a)(3), which is used in lieu of validating the refinement process. In the corresponding FAQs, AMS explains that testing finished ingredients for detectable modified genetic material is one way to validate the refining process. Other potential approaches include validation studies, experimental data applicable to in-plant operations, or applied data obtained during operational conditions.

   If evidence is available from other sources, additional data may not be required, though regulated entities would need to maintain a copy of the other source's evidence/data for their records. When evidence/data is applicable to multiple facilities or manufacturers, each would need to keep a copy as records.

6. **Continually verify the refinement process is operating as validated.** Verification requires monitoring that identified parameters of the key step(s) are operating as intended and validated. Regulated entities should establish a system, including frequency, for monitoring the parameters and record those measurements. In the FAQs, AMS explains that in most cases, the quality control procedures many regulated entities already have in place are sufficient for monitoring a refining process under the rule. The FAQ states, "USDA encourages regulated entities to establish their own monitoring protocols, such as observation of monitoring activities, review of records, and, in some cases, ongoing analytical tests."

7. **Revalidate the refinement process, as applicable, if significant changes are made to the process.** AMS clarifies that minor changes that do not affect key parameters would not need to be revalidated.

8. **Maintain record(s) of the validation and ongoing verification.** Regulated entities must maintain records for at last two years beyond the date the food or food product is sold or distributed for retail sale. AMS identifies third-party certifications, laboratory testing results, and validated process verification as examples of customary or reasonable records to demonstrate compliance with the disclosure requirements.

AMS also makes several important clarifications in the corresponding FAQs.

- AMS explains that there is no limit of detection for rDNA in a finished ingredient under the NBFDS, and the agency recognizes that testing methodologies may evolve so that in the future a test may have a lower limit of detection than current tests. If, in the future, modified genetic material in a food becomes detectable, the food ingredient would be subject to a bioengineered food disclosure. However, a process validated in compliance with the regulations will remain valid as long as the regulated entity does not make significant changes to the process. In these limited circumstances, the detectability of modified genetic

material is determined at the time of validation and there is no "moving target" associated with the emergence of new testing capabilities.

- AMS clarifies that regulated entities are not required to validate each key step in a process, nor are they required to identify the point at which modified genetic material becomes undetectable. Instead, they can validate that by the time an ingredient produced from a bioengineered crop reaches a certain key step, the modified genetic material has been rendered undetectable. If further process steps exist after the key step that is chosen, those additional steps must not re-introduce detectable modified genetic material.

- Regulated entities may validate a common process used for multiple ingredients.

- In-house laboratories may validate a refining process.

- If another facility validates a refining process, a regulated entity does not need to revalidate the process when completed in a different facility.

- The allowance in the regulation for 5% inadvertent or technically unavoidable presence of modified genetic material does not apply when a regulated entity intends to use a highly refined bioengineered food ingredient but does not refine it to the point where modified genetic material is no longer detectable.

- Validation of a refining process is not required; it is simply one of several potential ways to demonstrate that modified genetic material is non-detectable. If a regulated entity is using a food that is or derived from a food on the AMS List of Bioengineered Foods, it must make a disclosure unless it maintains records demonstrating that modified genetic material is undetectable. AMS states, "If regulated entities do not have [such records] and do not want to create them, they must make a bioengineered food disclosure."

Detectability Testing

AMS's regulations require that analytical testing for purposes of detecting the presence of modified genetic material in refined foods must meet the following standards:

1. Laboratory quality assurance must ensure the validity and reliability of the test results;

2. Analytical method selection, validation, and verification must ensure that the testing method used is appropriate (fit for purpose) and that the laboratory can successfully perform the testing;

3. The demonstration of testing validity must ensure consistent accurate analytical performance; and

4. Method performance specifications must ensure analytical tests are sufficiently sensitive for the purposes of the detectability requirements of the regulations.

The Guidance on Testing Methods provides the following considerations for selecting a test method to confirm the absence of modified genetic material in a food or food ingredient.

- **Selecting a "Fit for Purpose" Test Method:** AMS advises regulated entities should consider whether a method is fit for purpose by assessing its suitability to determine whether a food ingredient contains detectable modified genetic material. AMS identifies the following factors as critical for ensuring a method is fit for purpose:
    - Specific to the analyte of interest;
    - Appropriate (validated) for the product/commodity being tested;
    - Accurate, precise, robust, reliable, and reproducible;
    - The applicable range for the measurement value (i.e., appropriate sensitivity); and
    - Accessible and practical for testing needs.

  These factors are very similar to those identified in the draft guidance, with the exception that the final guidance no longer refers to a limit of detection or limit of quantitation. In the FAQs, AMS explains that a limit of detection is the lowest amount or concentration of analyte in a sample which can be reliably detected, and it states that entities should use their best discretion when selecting a test method to ensure appropriate sensitivity.

  AMS also continues to advise that entities should either use methods validated by accepted international bodies or validate their own methods to detect modified genetic material, and the agency provides resources for developing an analytical scheme to determine the presence and nature of rDNA in a food or ingredient.

- **DNA-Based Methods:** AMS states that at this time, polymerase chain reaction (PCR) is the most widely used and commercially accepted test method for determining whether modified genetic material is detectable in a food or ingredient. The guidance states qualitative PCR testing will detect the presence or absence of modified DNA, and quantitative PCR testing will reveal how much modified DNA is detectable in a product. The final guidance no longer states a preference for quantitative (rather than qualitative) PCR, and in the corresponding FAQs it states the agency does not prescribe the use of a particular method, as long as it is fit for purpose and otherwise meets the regulatory criteria.

  AMS notes that for some matrices, broad-spectrum PCR may not be capable of detecting all single or multiple-genetic modification events and/or may be subject to false positives, and in such circumstances event-specific or construct-specific PCR tests may be necessary.

  AMS also notes that the use of PCR may be limited by PCR-inhibiting compounds and is dependent on isolation of high-quality DNA from a sample. AMS advises that laboratories must ensure that the method is validated for the specific matrix and adequately extracts DNA for each ingredient/matrix and should monitor PCR inhibition. In the FAQs, AMS also states that highly refined foods may contain lipids that interfere with a PCR reaction, and regulated entities must follow appropriate procedures or acceptable methods to remove PCR inhibiting compounds in the sample extraction process.

- **Emerging Technologies and Other Methods:** The guidance continues to state that other DNA-based methods that meet the criteria and are fit for purpose for detecting modified genetic material may be acceptable.

- **Laboratory Selection:** AMS continues to encourage the selection of a laboratory that adheres to the ISO 17025 standard, along with the requirements in 7 C.F.R. § 66.9(c).

- **Recordkeeping Requirements:** As in the draft guidance, AMS identifies the following as examples of customary or reasonable records that entities could use to demonstrate compliance with the disclosure requirements as they relate to detectability testing: supply chain records, supplier attestations, third-party certifications, laboratory testing results, validated process verifications, and other records generated in the normal course of business. Entities also may maintain certificates of analysis or other records of testing that confirm the absence of modified genetic material. AMS notes that records should include details corresponding with the factors for assessing whether a test method is fit for purpose. The guidance explains that if AMS conducts an audit or examination under 7 C.F.R. § 66.402, the agency does not intend to conduct independent testing of food products, but will look at a regulated entity's ingredient-specific records.

In the FAQs for the Guidance on Testing Methods, AMS clarifies the following:

- There are no sample size requirements; instead, regulated entities should follow recommendations for performance and validation criteria in Codex Alimentarius Commission document *CAC/GL 74-2010 Guidelines on Performance Criteria and Validation of Methods for Detection, Identification and Quantification of Specific DNA Sequences and Specific Proteins in Foods*.

- If a complaint is filed that a bioengineered food was not properly disclosed, AMS will look at the regulated entity's records to determine whether they complied with the disclosure requirements in the NBFDS. AMS will not test foods to determine compliance and will not rely solely on test results submitted in complaints.

* * *

We will continue to monitor AMS's implementation of the NBFDS. Should you have any questions or require assistance validating a refining process, please do not hesitate to contact us.