PETITION FILE FOR 7F8546

Authority: 33 U.S.C. 1231; 50 U.S.C. 191; 33 CFR 1.05–1, 6.04–1, 6.04–6, and 160.5; Department of Homeland Security Delegation No. 0170.1.

■ 2. Add § 165.T08–1014 to read as follows:

§ 165.T08–1014 Security Zone; Corpus Christi Ship Channel. Corpus Christi, TX.

(a) *Location.* The following area is a security zone:

(1) For LNG GOLAR TUNDRA transiting shoreward of the seaward extremity of the Aransas Pass Jetties in the Corpus Christi Ship Channel and La Quinta Channel, the waters within a 500 yards of LNG GOLAR TUNDRA while transiting until moored.

(2) The mooring basin bound by 27°52′53.38″ N, 097°16′20.66″ W on the northern shoreline; thence to 27°52′45.58″ N, 097°16′19.60″ W; thence to 27°52′38.55″ N, 097°15′45.56″ W; thence to 27°52′49.30″ N, 097°15′45.44″ W; thence west along the shoreline to 27°52′53.38″ N, 097°16′20.66″ W, while LNG GOLAR TUNDRA is moored.

(b) *Effective/enforcement period.* This section is effective without actual notice from November 20, 2018 until November 21, 2018. For the purposes of enforcement, actual notice will be used from November 11, 2018 through November 20, 2018. Enforcement of this section began from the time LNG GOLAR TUNDRA entered the Corpus Christi Ship Channel on November 11, 2018 and will continue until LNG GOLAR TUNDRA's departure on or about November 21, 2018.

(c) *Regulations.* (1) The general regulations in § 165.33 of this part apply. Entry into these zones are prohibited unless authorized by the Captain of the Port Sector Corpus Christi (COTP) or a designated representative. A designated representative is a commissioned, warrant, or petty officer of the U.S. Coast Guard assigned to units under the operational control of USCG Sector Corpus Christi.

(2) Persons or vessels desiring to enter or pass through the zones must request permission from the COTP Sector Corpus Christi on VHF–FM channel 16 or by telephone at 361–939–0450.

(3) If permission is granted, all persons and vessels shall comply with the instructions of the COTP or designated representative.

(d) *Information broadcasts.* The COTP or a designated representative will inform the public through Broadcast Notices to Mariners (BNMs), Local Notices to Mariners (LNMs), and/or Marine Safety Information Bulletins (MSIBs) as appropriate of the enforcement times and date for these security zones.

Dated: November 9, 2018.

J.E. Smith,

Captain, U.S. Coast Guard, Acting Captain of the Port Sector Corpus Christi.

[FR Doc. 2018–25251 Filed 11–19–18; 8:45 am]

BILLING CODE 9110–04–P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Parts 51, 60, and 63

[EPA–HQ–OAR–2016–0510; FRL–9986–42–OAR]

RIN 2060–AS95

Revisions to Testing Regulations for Air Emission Sources

Correction

In rule document 2018–24747, appearing on pages 56713 through 56734 in the issue of Wednesday, November 14, 2018 make the following correction:

■ On page 56732, the asterisks directly above Eq. 323–8 were printed in error and those after were omitted. The equation is corrected to appear as set forth below:

Appendix A to Part 63 [Corrected]

Method 323-Measurment of Formaldehyde Emissions From Natural Gas-Fired Stationary Sources-Acetyl Acetone Derivitization Method

* * * * *

$$C_{form@15\%O_2} = C_{form}\frac{(20.9-15)}{(20.9-O_{2d})} \qquad \text{Eq. 323-8}$$

* * * * *

[FR Doc. C1–2018–24747 Filed 11–19–18; 8:45 am]

BILLING CODE 1301–00–D

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA–HQ–OPP–2017–0460; FRL–9985–98]

Bacillus amyloliquefaciens strain ENV503; Exemption From the Requirement of a Tolerance

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes an exemption from the requirement of a tolerance for residues of *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities when this pesticide chemical is used in accordance with label directions and good agricultural practices. Envera, LLC submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting an exemption from the requirement of a tolerance. This regulation eliminates the need to establish a maximum permissible level for residues of *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities under FFDCA.

DATES: This regulation is effective November 20, 2018. Objections and requests for hearings must be received on or before January 22, 2019, and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA–HQ–OPP–2017–0460, is available at *http://www.regulations.gov* or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the Environmental Protection Agency Docket Center (EPA/DC), West William Jefferson Clinton Bldg., Rm. 3334, 1301 Constitution Ave. NW, Washington, DC 20460–0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566–1744, and the telephone number for the OPP Docket is (703) 305–5805. Please review the visitor instructions and additional information about the docket available at *http://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT: Robert McNally, Biopesticides and Pollution Prevention Division (7511P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave. NW, Washington, DC 20460–0001; main telephone number: (703) 305–7090; email address: *BPPDFRNotices@epa.gov.*

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. How can I get electronic access to other related information?

You may access a frequently updated electronic version of 40 CFR part 180 through the Government Printing Office's e-CFR site at *http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl.*

C. How can I file an objection or hearing request?

Under FFDCA section 408(g), 21 U.S.C. 346a(g), any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA–HQ–OPP–2017–0460 in the subject line on the first page of your submission. All objections and requests for a hearing must be in writing, and must be received by the Hearing Clerk on or before January 22, 2019. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI)) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request, identified by docket ID number EPA–HQ–OPP–2017–0460, by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be CBI or other information whose disclosure is restricted by statute.
- *Mail:* OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave. NW, Washington, DC 20460–0001.
- *Hand Delivery:* To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.html.* Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets.*

II. Background

In the **Federal Register** of December 15, 2017 (82 FR 59604) (FRL–9970–50), EPA issued a document pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide tolerance petition (PP 7F8546) by Envera, LLC, 220 Garfield Ave., West Chester, PA 19380. The petition requested that 40 CFR part 180 be amended by establishing an exemption from the requirement of a tolerance for residues of the bactericide and fungicide *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities. That document referenced a summary of the petition prepared by the petitioner Envera, LLC and available in the docket via *http://www.regulations.gov.* Comments were received on the notice of filing. EPA's response to these comments is discussed in Unit III.C.

III. Final Rule

A. EPA's Safety Determination

Section 408(c)(2)(A)(i) of FFDCA allows EPA to establish an exemption from the requirement of a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the exemption is "safe." Section 408(c)(2)(A)(ii) of FFDCA defines "safe" to mean that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." This includes exposure through drinking water and in residential settings but does not include occupational exposure. Pursuant to FFDCA section 408(c)(2)(B), in establishing or maintaining in effect an exemption from the requirement of a tolerance, EPA must take into account the factors set forth in FFDCA section 408(b)(2)(C), which require EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance or tolerance exemption and to "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue. . . ." Additionally, FFDCA section 408(b)(2)(D) requires that EPA consider "available information concerning the cumulative effects of [a particular pesticide's] . . . residues and other substances that have a common mechanism of toxicity."

EPA evaluated the available toxicological and exposure data on *Bacillus amyloliquefaciens* strain ENV503 and the available toxicological data on *Bacillus subtilis* strain GB03, a microorganism that is genetically identical to *Bacillus amyloliquefaciens* strain ENV503, and considered their validity, completeness, and reliability, as well as the relationship of this information to human risk. A full explanation of the data upon which EPA relied and its risk assessment based on those data can be found within the document entitled "Federal Food, Drug, and Cosmetic Act (FFDCA) Safety Determination for *Bacillus amyloliquefaciens* strain ENV503" (Safety Determination). This document, as well as other relevant information, is available in the docket for this action as described under **ADDRESSES**.

The available data demonstrated that, with regard to humans, *Bacillus amyloliquefaciens* strain ENV503 is not toxic, pathogenic, or infective via any route of exposure. Although there may be some exposure to residues when *Bacillus amyloliquefaciens* strain ENV503 is used on all food commodities in accordance with label directions and good agricultural practices, such exposure is unlikely to significantly increase exposure above the background levels of *Bacillus amyloliquefaciens* organisms naturally present on food commodities. EPA also determined in the Safety Determination that retention of the Food Quality Protection Act (FQPA) safety factor was not necessary as part of the qualitative assessment conducted for *Bacillus amyloliquefaciens* strain ENV503.

Based upon its evaluation in the Safety Determination, EPA concludes that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of *Bacillus amyloliquefaciens* strain ENV503. Therefore, an exemption from the requirement of a tolerance is

established for residues of *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities when this pesticide chemical is used in accordance with label directions and good agricultural practices.

B. Analytical Enforcement Methodology

An analytical method is not required because EPA is establishing an exemption from the requirement of a tolerance without any numerical limitation.

C. Response to Comments

Four comments were received in response to the notice of filing. EPA reviewed the comments and determined that they are irrelevant to the tolerance exemption in this action.

IV. Statutory and Executive Order Reviews

This action establishes a tolerance exemption under FFDCA section 408(d) in response to a petition submitted to EPA. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled "Regulatory Planning and Review" (58 FR 51735, October 4, 1993). Because this action has been exempted from review under Executive Order 12866, this action is not subject to Executive Order 13211, entitled "Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use" (66 FR 28355, May 22, 2001), or Executive Order 13045, entitled "Protection of Children from Environmental Health Risks and Safety Risks" (62 FR 19885, April 23, 1997), nor is it considered a regulatory action under Executive Order 13771, entitled "Reducing Regulations and Controlling Regulatory Costs" (82 FR 9339, February 3, 2017). This action does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (44 U.S.C. 3501 *et seq.*) nor does it require any special considerations under Executive Order 12898, entitled "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations" (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerance exemption in this action, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (5 U.S.C. 601 *et seq.*) do not apply.

This action directly regulates growers, food processors, food handlers, and food retailers, not States or tribes. As a result, this action does not alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCA section 408(n)(4). As such, EPA has determined that this action will not have a substantial direct effect on States or tribal governments, on the relationship between the national government and the States or tribal governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian tribes. Thus, EPA has determined that Executive Order 13132, entitled "Federalism" (64 FR 43255, August 10, 1999), and Executive Order 13175, entitled "Consultation and Coordination with Indian Tribal Governments" (65 FR 67249, November 9, 2000), do not apply to this action. In addition, this action does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act (2 U.S.C. 1501 *et seq.*).

This action does not involve any technical standards that would require EPA's consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act (15 U.S.C. 272 note).

V. Congressional Review Act

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq.*), EPA will submit a report containing this rule and other required information to the U.S. Senate, the U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This action is not a "major rule" as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests, Reporting and recordkeeping requirements.

Dated: November 5, 2018.

Richard P. Keigwin, Jr.,

Director, Office of Pesticide Programs.

Therefore, 40 CFR chapter I is amended as follows:

PART 180—[AMENDED]

■ 1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

■ 2. Add § 180.1363 to subpart D to read as follows:

§ 180.1363 *Bacillus amyloliquefaciens* strain ENV503; exemption from the requirement of a tolerance.

An exemption from the requirement of a tolerance is established for residues of *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities when used in accordance with label directions and good agricultural practices.

[FR Doc. 2018–25313 Filed 11–19–18; 8:45 am]

BILLING CODE 6560–50–P

BILLING CODE 6560-50-P

ENVIRONMENTAL PROTECTION AGENCY

40 CFR Part 180

[EPA-HQ-OPP-2017-0460; FRL-9985-98]

***Bacillus amyloliquefaciens* strain ENV503; Exemption from the Requirement of a Tolerance**

AGENCY: Environmental Protection Agency (EPA).

ACTION: Final rule.

SUMMARY: This regulation establishes an exemption from the requirement of a tolerance for residues of *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities when this pesticide chemical is used in accordance with label directions and good agricultural practices. Envera, LLC submitted a petition to EPA under the Federal Food, Drug, and Cosmetic Act (FFDCA), requesting an exemption from the requirement of a tolerance. This regulation eliminates the need to establish a maximum permissible level for residues of *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities under FFDCA.

DATES: This regulation is effective [*insert date of publication in the* **Federal Register**]. Objections and requests for hearings must be received on or before [*insert date 60 days after date of publication in the* **Federal Register**], and must be filed in accordance with the instructions provided in 40 CFR part 178 (see also Unit I.C. of the **SUPPLEMENTARY INFORMATION**).

ADDRESSES: The docket for this action, identified by docket identification (ID) number EPA-HQ-OPP-2017-0460, is available at *http://www.regulations.gov* or at the Office of Pesticide Programs Regulatory Public Docket (OPP Docket) in the

Environmental Protection Agency Docket Center (EPA/DC), West William Jefferson Clinton Bldg., Rm. 3334, 1301 Constitution Ave., NW., Washington, DC 20460-0001. The Public Reading Room is open from 8:30 a.m. to 4:30 p.m., Monday through Friday, excluding legal holidays. The telephone number for the Public Reading Room is (202) 566-1744, and the telephone number for the OPP Docket is (703) 305-5805. Please review the visitor instructions and additional information about the docket available at *http://www.epa.gov/dockets*.

FOR FURTHER INFORMATION CONTACT: Robert McNally, Biopesticides and Pollution Prevention Division (7511P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001; main telephone number: (703) 305-7090; email address: *BPPDFRNotices@epa.gov*.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this Action Apply to Me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

B. How Can I Get Electronic Access to Other Related Information?

You may access a frequently updated electronic version of 40 CFR part 180 through the Government Printing Office's e-CFR site at *http://www.ecfr.gov/cgi-bin/text-idx?&c=ecfr&tpl=/ecfrbrowse/Title40/40tab_02.tpl.*

C. How Can I File an Objection or Hearing Request?

Under FFDCA section 408(g), 21 U.S.C. 346a(g), any person may file an objection to any aspect of this regulation and may also request a hearing on those objections. You must file your objection or request a hearing on this regulation in accordance with the instructions provided in 40 CFR part 178. To ensure proper receipt by EPA, you must identify docket ID number EPA-HQ-OPP-2017-0460 in the subject line on the first page of your submission. All objections and requests for a hearing must be in writing, and must be received by the Hearing Clerk on or before [*insert date 60 days after date of publication in the* **Federal Register**]. Addresses for mail and hand delivery of objections and hearing requests are provided in 40 CFR 178.25(b).

In addition to filing an objection or hearing request with the Hearing Clerk as described in 40 CFR part 178, please submit a copy of the filing (excluding any Confidential Business Information (CBI)) for inclusion in the public docket. Information not marked confidential pursuant to 40 CFR part 2 may be disclosed publicly by EPA without prior notice. Submit the non-CBI copy of your objection or hearing request, identified by docket ID number EPA-HQ-OPP-2017-0460, by one of the following methods:

• *Federal eRulemaking Portal*: *http://www.regulations.gov*. Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be CBI or other information whose disclosure is restricted by statute.

• *Mail*: OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave., NW., Washington, DC 20460-0001.

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II. Background

In the **Federal Register** of December 15, 2017 (82 FR 59604) (FRL-9970-50), EPA issued a document pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide tolerance petition (PP 7F8546) by Envera, LLC, 220 Garfield Ave., West Chester, PA 19380. The petition requested that 40 CFR part 180 be amended by establishing an exemption from the requirement of a tolerance for residues of the bactericide and fungicide *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities. That document referenced a summary of the petition prepared by the petitioner Envera, LLC and available in the docket via *http://www.regulations.gov*. Comments were received on the notice of filing. EPA's response to these comments is discussed in Unit III.C.

III. Final Rule

A. EPA's Safety Determination

Section 408(c)(2)(A)(i) of FFDCA allows EPA to establish an exemption from the requirement of a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the exemption is "safe." Section 408(c)(2)(A)(ii) of FFDCA defines "safe" to mean that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." This includes exposure through drinking water and in residential settings but does not include occupational exposure. Pursuant to FFDCA section 408(c)(2)(B), in establishing or maintaining in effect an exemption from the requirement of a tolerance, EPA must take into account the factors set forth in FFDCA section 408(b)(2)(C), which require EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance or tolerance exemption and to "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue. . . ." Additionally, FFDCA section 408(b)(2)(D) requires that EPA consider "available information concerning the cumulative effects of [a particular pesticide's] . . . residues and other substances that have a common mechanism of toxicity."

EPA evaluated the available toxicological and exposure data on *Bacillus amyloliquefaciens* strain ENV503 and the available toxicological data on *Bacillus subtilis* strain GB03, a microorganism that is genetically identical to *Bacillus amyloliquefaciens* strain ENV503, and considered their validity, completeness, and reliability, as well as the relationship of this information to human risk. A full explanation of the data upon which EPA relied and its risk assessment based on those data can be found within the document

entitled "Federal Food, Drug, and Cosmetic Act (FFDCA) Safety Determination for *Bacillus amyloliquefaciens* strain ENV503" (Safety Determination). This document, as well as other relevant information, is available in the docket for this action as described under **ADDRESSES**.

The available data demonstrated that, with regard to humans, *Bacillus amyloliquefaciens* strain ENV503 is not toxic, pathogenic, or infective via any route of exposure. Although there may be some exposure to residues when *Bacillus amyloliquefaciens* strain ENV503 is used on all food commodities in accordance with label directions and good agricultural practices, such exposure is unlikely to significantly increase exposure above the background levels of *Bacillus amyloliquefaciens* organisms naturally present on food commodities. EPA also determined in the Safety Determination that retention of the Food Quality Protection Act (FQPA) safety factor was not necessary as part of the qualitative assessment conducted for *Bacillus amyloliquefaciens* strain ENV503.

Based upon its evaluation in the Safety Determination, EPA concludes that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of *Bacillus amyloliquefaciens* strain ENV503. Therefore, an exemption from the requirement of a tolerance is established for residues of *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities when this pesticide chemical is used in accordance with label directions and good agricultural practices.

B. Analytical Enforcement Methodology

An analytical method is not required because EPA is establishing an exemption from the requirement of a tolerance without any numerical limitation.

C. Response to Comments

Four comments were received in response to the notice of filing. EPA reviewed the comments and determined that they are irrelevant to the tolerance exemption in this action.

IV. Statutory and Executive Order Reviews

This action establishes a tolerance exemption under FFDCA section 408(d) in response to a petition submitted to EPA. The Office of Management and Budget (OMB) has exempted these types of actions from review under Executive Order 12866, entitled "Regulatory Planning and Review" (58 FR 51735, October 4, 1993). Because this action has been exempted from review under Executive Order 12866, this action is not subject to Executive Order 13211, entitled "Actions Concerning Regulations That Significantly Affect Energy Supply, Distribution, or Use" (66 FR 28355, May 22, 2001), or Executive Order 13045, entitled "Protection of Children from Environmental Health Risks and Safety Risks" (62 FR 19885, April 23, 1997), nor is it considered a regulatory action under Executive Order 13771, entitled "Reducing Regulations and Controlling Regulatory Costs" (82 FR 9339, February 3, 2017). This action does not contain any information collections subject to OMB approval under the Paperwork Reduction Act (44 U.S.C. 3501 *et seq.*) nor does it require any special considerations under Executive Order 12898, entitled "Federal Actions to Address Environmental Justice in Minority Populations and Low-Income Populations" (59 FR 7629, February 16, 1994).

Since tolerances and exemptions that are established on the basis of a petition under FFDCA section 408(d), such as the tolerance exemption in this action, do not require the issuance of a proposed rule, the requirements of the Regulatory Flexibility Act (5 U.S.C. 601 *et seq.*) do not apply.

This action directly regulates growers, food processors, food handlers, and food retailers, not States or tribes. As a result, this action does not alter the relationships or distribution of power and responsibilities established by Congress in the preemption provisions of FFDCA section 408(n)(4). As such, EPA has determined that this action will not have a substantial direct effect on States or tribal governments, on the relationship between the national government and the States or tribal governments, or on the distribution of power and responsibilities among the various levels of government or between the Federal Government and Indian tribes. Thus, EPA has determined that Executive Order 13132, entitled "Federalism" (64 FR 43255, August 10, 1999), and Executive Order 13175, entitled "Consultation and Coordination with Indian Tribal Governments" (65 FR 67249, November 9, 2000), do not apply to this action. In addition, this action does not impose any enforceable duty or contain any unfunded mandate as described under Title II of the Unfunded Mandates Reform Act (2 U.S.C. 1501 *et seq.*).

This action does not involve any technical standards that would require EPA's consideration of voluntary consensus standards pursuant to section 12(d) of the National Technology Transfer and Advancement Act (15 U.S.C. 272 note).

V. Congressional Review Act

Pursuant to the Congressional Review Act (5 U.S.C. 801 *et seq.*), EPA will submit a report containing this rule and other required information to the U.S. Senate, the

U.S. House of Representatives, and the Comptroller General of the United States prior to publication of the rule in the **Federal Register**. This action is not a "major rule" as defined by 5 U.S.C. 804(2).

List of Subjects in 40 CFR Part 180

Environmental protection, Administrative practice and procedure, Agricultural commodities, Pesticides and pests. Reporting and recordkeeping requirements.

Dated: 11/5/2018

Richard P. Keigwin, Jr.,
Director, Office of Pesticide Programs.

Therefore, 40 CFR chapter I is amended as follows:

PART 180--[AMENDED]

1. The authority citation for part 180 continues to read as follows:

Authority: 21 U.S.C. 321(q), 346a and 371.

2. Add § 180.1363 to subpart D to read as follows:

§180.1363 *Bacillus amyloliquefaciens* strain ENV503; exemption from the requirement of a tolerance.

An exemption from the requirement of a tolerance is established for residues of *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities when used in accordance with label directions and good agricultural practices

Federal Food, Drug, and Cosmetic Act (FFDCA) Safety Determination for *Bacillus amyloliquefaciens* strain ENV503

Docket ID Number: EPA-HQ-OPP-2017-0460

Approved by:

Richard P. Keigwin, Jr., Director
Office of Pesticide Programs
U.S. Environmental Protection Agency

Date:

11/5/2018

I. Introduction

Section 408(c)(2)(A)(i) of FFDCA allows the U.S. Environmental Protection Agency (EPA) to establish an exemption from the requirement of a tolerance (the legal limit for a pesticide chemical residue in or on a food) only if EPA determines that the exemption is "safe." Section 408(c)(2)(A)(ii) of FFDCA defines "safe" to mean that "there is a reasonable certainty that no harm will result from aggregate exposure to the pesticide chemical residue, including all anticipated dietary exposures and all other exposures for which there is reliable information." This includes exposure through drinking water and in residential settings but does not include occupational exposure. Pursuant to FFDCA section 408(c)(2)(B), in establishing or maintaining in effect an exemption from the requirement of a tolerance, EPA must take into account the factors set forth in FFDCA section 408(b)(2)(C), which require EPA to give special consideration to exposure of infants and children to the pesticide chemical residue in establishing a tolerance or tolerance exemption and to "ensure that there is a reasonable certainty that no harm will result to infants and children from aggregate exposure to the pesticide chemical residue. . . ." Additionally, FFDCA section 408(b)(2)(D) requires that EPA consider "available information concerning the cumulative effects of [a particular pesticide's] . . . residues and other substances that have a common mechanism of toxicity."

EPA performs a number of analyses to determine the risks from aggregate exposure to pesticide residues. First, for microbial pesticides, EPA determines the pathogenicity and toxicity potential of the pesticide. Second, EPA examines exposure to the pesticide through food, drinking water, and other exposures that occur as a result of pesticide use in residential settings, as well as other non-occupational exposure to the substance.

II. Summary of Petitioned-for Tolerance Exemption

In the Federal Register of December 15, 2017 (82 FR 59604), EPA issued a document pursuant to FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), announcing the filing of a pesticide tolerance petition (PP 7F8546) by Envera, LLC, 220 Garfield Ave., West Chester, PA 19380. The petition requested that 40 CFR part 180 be amended by establishing an exemption from the requirement of a tolerance for residues of the bactericide and fungicide *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities. That document referenced a summary of the petition prepared by the petitioner Envera, LLC and is available in Docket ID Number EPA-HQ-OPP-2017-0460 via www.regulations.gov.

III. Toxicological Profile

Consistent with FFDCA section 408(b)(2)(D), EPA reviewed the available scientific data and other relevant information on *Bacillus amyloliquefaciens* strain ENV503 and considered their validity, completeness, and reliability, as well as the relationship of this information to human risk. EPA also considered available information concerning the variability of the sensitivities of major identifiable subgroups of consumers, including infants and children.

A. Overview of Bacillus amyloliquefaciens, **including strain ENV503 (Ref. 1)**

Bacillus amyloliquefaciens is a rod-shaped, Gram-positive, non-pathogenic, aerobic bacterium that is ubiquitous in nature and that has been recovered from water, soil, air, and decomposing plant material. A strain of *Bacillus amyloliquefaciens*, ENV503, is proposed for use as a microbial active ingredient in pesticide products and is intended to prevent, control, or suppress many soilborne and foliar diseases, both fungal and bacterial. When applied as a pesticide, *Bacillus amyloliquefaciens* strain ENV503 establishes beneficial colonies on the roots and leaves of plants, thereby protecting plant roots from invading

pathogens, stimulating healthier plant roots, improving nutrient uptake, and triggering a natural immune response in plants that results in Induced Systemic Resistance to certain pathogens.

Bacillus amyloliquefaciens strain ENV503 is genetically identical to *Bacillus subtilis* strain GB03, a microorganism that is the active ingredient in two currently registered pesticide products. It was first registered in pesticide products on July 9, 1992, and has a tolerance exemption established under 40 CFR § 180.1111. EPA determined *Bacillus amyloliquefaciens* strain ENV503 to be genetically identical to *Bacillus subtilis* strain GB03 through the review of nucleotide sequence analysis provided by the petitioner.

B. Microbial Pesticide Toxicology Data Requirements

Because the petitioner provided data that show *Bacillus amyloliquefaciens* strain ENV503 and *Bacillus subtilis* strain GB03 are identical, as well as a bridging study that demonstrated no toxicity, pathogenicity, or infectivity attributed to *Bacillus amyloliquefaciens* strain ENV503, EPA concludes that the active ingredient data done with *Bacillus subtilis* strain GB03, which were cited by the petitioner, are representative of the toxicological nature of *Bacillus amyloliquefaciens* strain ENV503. In addition to the data generated by the petitioner, these *Bacillus subtilis* strain GB03 data support the requested tolerance exemption and are summarized immediately below.

The toxicological profile of *Bacillus subtilis* strain GB03, which, again, is considered to be reflective of the toxicological profile of *Bacillus amyloliquefaciens* strain ENV503 based on the data provided by the petitioner, was described extensively in the Federal Register of August 27, 2008 (73 FR 50553). Those health effects data were the basis for establishing the tolerance exemption for *Bacillus subtilis* strain GB03 in or on all raw agricultural commodities. The supporting studies tested the toxicity/pathogenicity of *Bacillus subtilis* strain GB03 through acute oral (MRID No. 418123-02; Harmonized Guideline 885.3050), pulmonary (MRID No. 418123-04; Harmonized Guideline 885.3150), and injection (MRID No. 418123-05; Harmonized Guideline 885.3200) exposures and did not indicate any evidence of toxicity, pathogenicity, or infectivity. Further, when exposed via injection, a distinct pattern of clearance was demonstrated in the test animals. Finally, in an acute dermal toxicity test (MRID No. 418123-03; Harmonized Guideline 870.1200), *Bacillus subtilis* strain GB03 was not considered to be toxic.[1]

To allow bridging of the *Bacillus subtilis* strain GB03 data summarized above to support this tolerance exemption, the petitioner also provided an acute injection toxicity/pathogenicity test done with *Bacillus amyloliquefaciens* strain ENV503 (MRID No. 505038-01; Harmonized Guideline 885.3200). This acceptable study demonstrated that *Bacillus amyloliquefaciens* strain ENV503 was not toxic, pathogenic, or infective to rats when injected intravenously at a dose of 2.5×10^8 colony-forming units (CFU)/mL or 2.5×10^7 CFU/rat. A steady diminishment of viable CFU counts was demonstrated in all the organs tested with bacterial counts at, near, or below the limits of detection on day 42, the last day of this study.

IV. Aggregate Exposure (Ref. 1)

In examining aggregate exposure, FFDCA section 408 directs EPA to consider available information concerning exposures from the pesticide residue in food and all other non-occupational exposures, including drinking water from ground water or surface water and exposure through pesticide use in gardens, lawns, or buildings (residential and other indoor uses).

[1] The acute dermal toxicity study for *Bacillus subtilis* strain GB03 was incorrectly described as Toxicity Category III in the August 27, 2008, Federal Register document. According to the data submitted by the petitioner and reviewed by EPA, the appropriate classification for the acute dermal toxicity study is Toxicity Category IV (see Section III of Ref. 2 for a description of Toxicity Categories).

Based on the lack of toxicity, infectivity, or pathogenicity in the available data, EPA has not identified any toxicological endpoints. Therefore, EPA's aggregate assessment of *Bacillus amyloliquefaciens* strain ENV503 is qualitative, rather than quantitative, in nature.

Food Exposure: Based on the proposed uses for the end-use product, exposure to *Bacillus amyloliquefaciens* strain ENV503 through food commodities is possible. *Bacillus amyloliquefaciens* group strains are ubiquitous in nature and are commonly found on various types of fresh produce. Since *Bacillus amyloliquefaciens* strain ENV503 is included in the end-use product at only 0.15% and the end-use product is applied at relatively low concentrations, it is unlikely that residues would result in a significant increase in exposure above the background levels of *Bacillus amyloliquefaciens* organisms naturally present on food commodities. Should *Bacillus amyloliquefaciens* strain ENV503 be present in or on food, it is not expected to be toxic, pathogenic, or infective, given the toxicological data provided or cited by the petitioner and other information known to EPA (e.g., *Bacillus amyloliquefaciens* group strains not being associated with foodborne disease outbreaks or production of mammalian toxins).

Drinking Water Exposure: Based on the proposed uses for the end-use product, exposure to *Bacillus amyloliquefaciens* strain ENV503 through drinking water is possible. *Bacillus amyloliquefaciens* group strains are ubiquitous in nature and have been recovered from water. According to the World Health Organization, *Bacillus* species are often detected in drinking water even after going through acceptable water treatment processes, largely because the spores are resistant to drinking water disinfection processes (Ref. 3). *Bacillus amyloliquefaciens* strain ENV503, however, is not intended for application to surface or ground water, *Bacillus amyloliquefaciens* strain ENV503 is present in the end-use product at only 0.15%, and the end-use product is applied at relatively low concentrations. Considering all of these factors, EPA believes that it is unlikely that residues would result in a significant increase in exposure above the background levels of *Bacillus amyloliquefaciens* organisms that may be naturally present in water. Should *Bacillus amyloliquefaciens* strain ENV503 be present in drinking water, it is not expected to be toxic, pathogenic, or infective, given the toxicological data provided or cited by the petitioner.

Other Non-Occupational Exposure: Although *Bacillus amyloliquefaciens* strain ENV503 is intended primarily for agricultural/commercial use sites, the end-use product is proposed for use on grasses grown for seed and for sod production. As a result, planting of treated grass seed or sod in residential/commercial areas could potentially result in indirect non-occupational dermal exposure. These uses, however, are not expected to result in a significant increase in exposure above the background environmental levels of *Bacillus amyloliquefaciens* organisms. Should indirect dermal exposure occur through treated turf grass seed or sod or the uses of *Bacillus amyloliquefaciens* strain ENV503 be expanded in the future such that other exposures would occur (e.g., direct inhalation and dermal exposures, as a result of EPA-permitted applications in home gardens), the toxicological data provided by the petitioner demonstrated a lack of significant toxicity, infectivity, pathogenicity, or other adverse effects.

V. Cumulative Effects from Substances with a Common Mechanism of Toxicity

Section 408(b)(2)(D)(v) of FFDCA requires that, when considering whether to establish, modify, or revoke a tolerance, EPA consider "available information concerning the cumulative effects of [a particular pesticide's] . . . residues and other substances that have a common mechanism of toxicity."

Bacillus amyloliquefaciens strain ENV503 is not toxic in humans and does not have a common mechanism of human toxicity with other substances. Consequently, FFDCA section 408(b)(2)(D)(v) does not apply.

VI. Determination of Safety for the U.S. Population, Infants, and Children

A. U.S. Population

Due to the lack of toxicity, pathogenicity, or infectivity of *Bacillus amyloliquefaciens* strain ENV503, EPA concludes that there is reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of *Bacillus amyloliquefaciens* strain ENV503. This includes all anticipated dietary exposures and all other exposures for which there is reliable information.

B. Infants and Children

FFDCA section 408(b)(2)(C) provides that EPA shall apply an additional tenfold (10X) margin of safety for infants and children in the case of threshold effects to account for prenatal and postnatal toxicity and the completeness of the database on toxicity and exposure, unless EPA determines based on reliable data that a different margin of safety will be safe for infants and children. This additional margin of safety is commonly referred to as the Food Quality Protection Act Safety Factor. In applying this provision, EPA either retains the default value of 10X or uses a different additional safety factor when reliable data available to EPA support the choice of a different factor.

As discussed above, EPA has concluded that *Bacillus amyloliquefaciens* strain ENV503 is not toxic, pathogenic, or infective to mammals, including infants and children. Because there are no threshold levels of concern to infants, children, and adults when *Bacillus amyloliquefaciens* strain ENV503 is used according to label directions and good agricultural practices, EPA concludes that no additional margin of safety is necessary to protect infants and children.

VII. Conclusions

EPA concludes that there is a reasonable certainty that no harm will result to the U.S. population, including infants and children, from aggregate exposure to residues of *Bacillus amyloliquefaciens* strain ENV503. Therefore, an exemption from the requirement of a tolerance can be established for residues of *Bacillus amyloliquefaciens* strain ENV503 in or on all food commodities when this pesticide chemical is used in accordance with label directions and good agricultural practices.

VIII. References

1. U.S. EPA. 2018a. *Bacillus amyloliquefaciens* strain ENV503 (PC Code 129287) – Human Health Risk Assessment Summary. Memorandum from M. Perry through J. Kough, Ph.D. and S. Borges to A. Boukedes; dated September 10, 2018 (available as a "Supporting Document" within Docket ID Number EPA-HQ-OPP-2017-0461 at www.regulations.gov)

2. U.S. EPA. 2018b. Chapter 7 of the Label Review Manual (Precautionary Statements) (Revised March 2018). Available from www.epa.gov/sites/production/files/2018-04/documents/chap-07-mar-2018.pdf.

3. World Health Organization. 2011. Guidelines for drinking-water quality. 4th Edition. Available from www.who.int/water_sanitation_health/publications/2011/dwq_guidelines/en/.

PRIA Renegotiation Form

Decision	Registration Number	Petition
526002	87645-G	
526004	87645-U	
526005		7F8546

Chemical Name	Bacillus amyloliquefaciens strain ENV503
Company Name	Envera, LLC
Fee Category	B590
PRIA Decision Time Frame	17M
Original PRIA Due Date	2018-08-02
Proposed New PRIA Due Date	2018-12-18
Previous Negotiated Dates	2018-11-08

Negotiated Due Date Reason

Additional Data Required:

☐ Product Chemistry ☐ Toxicology ☐ Acute Tox ☐ Environmental ☐ Efficacy ☐ Ecological ☐ Residue ☐ Other

Comments:

Data Deficiencies:

☐ Product Chemistry ☐ Toxicology ☐ Acute Tox ☐ Environmental ☐ Efficacy ☐ Ecological ☐ Residue ☐ Labeling ☐ Other ☐ Not Submitted

Comments:

Late Risk Assessment:

☐ Human Health ☐ Ecological

Interim Considerations:

[X] Agency Initiated [ ] Registrant Initiated

[X] 86-5 Deficiencies need to be addressed [X] Endangered Species Concerns [ ] Data Not Submitted [ ] Failure to Respond to Deficiencies [X] Other - Comment Field [ ] Risk Issues Environmental [ ] Risk Issues Human Health [ ] CSF [ ] Label [X] Public Process [ ] Impurities Review [ ] Administrative-FR Notice

Summary of Deficiency Type(s)

[X] Agency Initiated [ ] Registrant Initiated

Is "Fix" in-house? Yes

Describe Interactions with Company(Describe when Contacted and Company's Response including response to Previous Negotiated Due Dates:)

As stated in the previous negotiation form for these applications, EPA spent a good deal of the PRIA timeframe communicating with the applicant about deficiencies that needed to be addressed before completion of the comprehensive risk assessments. Indeed, EPA sent four official deficiency-related correspondences to the applicant: one 10-day deficiency letter, one response to a preliminary response to a 75-day deficiency letter, and two 75-day deficiency letters. During the previous negotiation process, EPA proposed to the applicant a new PRIA due date of December 18, 2018, given the anticipated timing of completion of the science reviews (mid-September 2018) and the regulatory tasks that needed to be completed after receipt of such science reviews. The applicant was unwilling to agree to a new PRIA due date past November 8, 2018, so EPA agreed to this date. Despite our best efforts, EPA is still working on some of the regulatory tasks and will not complete them before the current November 8, 2018, PRIA due date; therefore, EPA asked the applicant to negotiate the PRIA due date again. EPA and the applicant have agreed upon a new PRIA due date of December 18, 2018, i.e., the date that EPA initially proposed with the previous negotiation.

"75 Date" Letter Sent?	Yes
Date Sent	2018-04-04
Registrant Notified that this is the Last Negotiation?	NA

Rationale for Proposed Due Date: EPA needs to negotiate the PRIA due date from November 8, 2018, to December 18, 2018, to allow the following to be accomplished: - Publish the tolerance exemption in the Federal Register - Complete the final decision document - Issue registrations

Issue(s) Describe in Detail: See above in "Describe Interactions with Company" section.

Comment(s): Follow-up to 2018-11-08 email approval while system was down. Approval email is attached for the record.

Approved /Disapproved:	Approved
Date of Final Decision	Fri Nov 09 08:04:02 EST 2018 Richard Keigwin (RKEIGWIN) from IO (Host IP Address: 161.80.156.64)

e-Signature:

Richard Keigwin (RKEIGWIN) from IO (Host IP Address: 161.80.156.64)

Boukedes, Alexandra

From: Carlisle, Sharon
Sent: Thursday, November 8, 2018 2:38 PM
To: Boukedes, Alexandra
Subject: FW: Renegotiation for BAM ENV503

From: Carlisle, Sharon
Sent: Thursday, November 08, 2018 2:38 PM
To: Keigwin, Richard <Keigwin.Richard@epa.gov>; Ellis, Frank <Ellis.Frank@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: RE: Renegotiation for BAM ENV503

Thanks Rick – will do!

Thanks,

SharRon

703-308-6427
carlisle.sharon@epa.gov

From: Keigwin, Richard
Sent: Thursday, November 08, 2018 2:31 PM
To: Ellis, Frank <Ellis.Frank@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Carlisle, Sharon <Carlisle.Sharon@epa.gov>; Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: RE: Renegotiation for BAM ENV503

I approve the renegotiation. When the system comes back on line, we can put in through the formal system. In case the system doesn't come back on line today, let's PDF this email exchange and include it with the renegotiation through the formal system. I want to make sure that we have documentation that the renegotiation was completed prior to the PRIA clock expiring. Thanks!

From: Ellis, Frank
Sent: Thursday, November 08, 2018 2:24 PM
To: Keigwin, Richard <Keigwin.Richard@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Carlisle, Sharon <Carlisle.Sharon@epa.gov>; Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: Renegotiation for BAM ENV503
Importance: High

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Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Kausch, Jeannine <Kausch.Jeannine@epa.gov>
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SharRon

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carlisle.sharon@epa.gov

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Subject: RE: Renegotiation for BAM ENV503

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To: Keigwin, Richard <Keigwin.Richard@epa.gov>; Messina, Edward <Messina.Edward@epa.gov>
Cc: McNally, Robert <Mcnally.Robert@epa.gov>; Carlisle, Sharon <Carlisle.Sharon@epa.gov>; Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: Renegotiation for BAM ENV503
Importance: High

Because the renegotiation tracking system is down, BPPD is conveying the rationale for the renegotiation for BAM ENV503 and our concurrence through this email. The current due date is today (Nov. 8), and the proposed renegotiated date is Dec. 18, 2018. The company's concurrence on the renegotiation is attached.

Once the system comes back online, we can process electronically.

Frank Ellis | Acting Deputy Director | Biopesticides and Pollution Prevention Division
U.S. Environmental Protection Agency | 1200 Pennsylvania Ave NW (7511P) | Washington, DC 20460
(703) 308-8107

Renegotiation Rationale for Bacillus amyloliquefaciens ENV503 (87645-G, 87645-U, 7F8546)

Describe Interactions with Company (Describe when Contacted and Company's Response including response to Previous Negotiated Due Dates:

EPA spent a lot of time communicating with the applicant about deficiencies that needed to be addressed before completion of the comprehensive risk assessments. EPA had to send out four official correspondences (one 10-day deficiency letter, one response to a preliminary response to a 75-day deficiency letter, and two 75-day deficiency letters). This series of correspondence took about a year and caused EPA to renegotiate the PRIA date. During the first renegotiation process, EPA proposed a date of December 18, 2018. The applicant was resistant to renegotiating and did not accept the proposed date. Finally, EPA and the applicant agreed to a renegotiated date of November 8, 2018.

EPA needs to renegotiate a second time to complete the final registration steps. The applicant agreed to a new PRIA date of December 18, 2018.

Rationale for Proposed Due Date:

EPA needs to negotiate the PRIA due date from 11/08/2018 to 12/18/2018 to allow the following to be accomplished:

- Complete and sign the final decision document
- Publish the final rule tolerance exemption in the Federal Register
- Issue registrations

Because the renegotiation tracking system is down, BPPD is conveying the rationale for the renegotiation for BAM ENV503 and our concurrence through this email. The current due date is today (Nov. 8), and the proposed renegotiated date is Dec. 18, 2018. The company's concurrence on the renegotiation is attached.

Once the system comes back online, we can process electronically.

Frank Ellis | Acting Deputy Director | Biopesticides and Pollution Prevention Division
U.S. Environmental Protection Agency | 1200 Pennsylvania Ave NW (7511P) | Washington, DC 20460
(703) 308-8107

Renegotiation Rationale for Bacillus amyloliquefaciens ENV503 (87645-G, 87645-U, 7F8546)

Describe Interactions with Company (Describe when Contacted and Company's Response including response to Previous Negotiated Due Dates:

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EPA needs to negotiate the PRIA due date from 11/08/2018 to 12/18/2018 to allow the following to be accomplished:

- Complete and sign the final decision document
- Publish the final rule tolerance exemption in the Federal Register
- Issue registrations

Boukedes, Alexandra

From: Boukedes, Alexandra
Sent: Thursday, November 1, 2018 3:43 PM
To: Keeva Shultz
Cc: Kausch, Jeannine
Subject: RE: Bacillus amyloliquefaciens strain ENV503 (87645-G, 87645-U, and 7F8546) Second Renegotiated PRIA Date

Hi Keeva,

Thank you. I will keep you update on the status of the registration.

Thanks,
Alex

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-347-0305
boukedes.alexandra@epa.gov

From: Keeva Shultz [mailto:keeva@wagnerreg.com]
Sent: Thursday, November 1, 2018 7:14 AM
To: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Cc: Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: RE: Bacillus amyloliquefaciens strain ENV503 (87645-G, 87645-U, and 7F8546) Second Renegotiated PRIA Date

Hi Alex,

We agree to this PRIA extension.

Thank you,
Keeva Shultz

Wagner Regulatory Associates, Inc.
7217 Lancaster Pike, Suite A
Hockessin, DE 19707
302-635-7281
keeva@wagnerreg.com

This email and any files transmitted with it are confidential and intended solely for the use of the individual or entity to whom they are addressed. If you have received this email in error please notify the system manager. This message contains confidential information and is intended only for the individual named. If you are not the named addressee you should not disseminate, distribute or copy this e-mail. Please notify the sender immediately by e-mail if you have received this e-mail by mistake and delete this e-mail from your system. If you are not the intended recipient you are notified that disclosing, copying, distributing or taking any action in reliance on the contents of this information is strictly prohibited.

From: Boukedes, Alexandra [mailto:boukedes.alexandra@epa.gov]
Sent: Wednesday, October 31, 2018 2:39 PM
To: Keeva Shultz
Cc: Kausch, Jeannine
Subject: Bacillus amyloliquefaciens strain ENV503 (87645-G, 87645-U, and 7F8546) Second Renegotiated PRIA Date

Hi Keeva,

The current renegotiated PRIA date for the *Bacillus amyloliquefaciens* strain ENV503 (87645-G, 87645-U, and 7F8546) application is November 8, 2018. Although we have worked very hard, we will not make the November 8 date and need to renegotiate the PRIA date. We need time to complete the review of the tolerance exemption and get it signed by our office director, write the decision document and get it signed by our office director, and publish the final tolerance exemption rule in the Federal Register before we registered these products. To complete these steps we have to work with individuals internal and external to OPP and it takes time for these documents to move through the process.

We are proposing a renegotiated PRIA date of December 18, 2018. We do not believe we will use this entire time, but want to make sure we do not have to renegotiate the PRIA date a third time. Please let me know if you have any questions or would like to discuss this further.

Thanks,
Alex

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-347-0305
boukedes.alexandra@epa.gov

PRIA Renegotiation Form

Decision	Registration Number	Petition
526002	87645-G	
526004	87645-U	
526005		7F8546

Chemical Name	Bacillus amyloliquefaciens strain ENV503
Company Name	ENVERA, LLC
Fee Category	B590
PRIA Decision Time Frame	17M
Original PRIA Due Date	2018-08-02
Proposed New PRIA Due Date	2018-11-08
Previous Negotiated Dates	

Negotiated Due Date Reason

Additional Data Required:

☐ Product Chemistry ☐ Toxicology ☐ Acute Tox ☐ Environmental ☐ Efficacy ☐ Ecological ☐ Residue ☐ Other

Comments:

Data Deficiencies:

☐ Product Chemistry ☐ Toxicology ☐ Acute Tox ☐ Environmental ☐ Efficacy ☐ Ecological ☐ Residue ☐ Labeling ☐ Other ☐ Not Submitted

Comments:

Late Risk Assessment:

☐ Human Health ☐ Ecological

Interim Considerations:

[X] Agency Initiated [X] Registrant Initiated

[X] 86-5 Deficiencies need to be addressed [X] Endangered Species Concerns [ ] Data Not Submitted [ ] Failure to Respond to Deficiencies [X] Other - Comment Field [X] Risk Issues Environmental [ ] Risk Issues Human Health [ ] CSF [ ] Label [X] Public Process [ ] Impurities Review [ ] Administrative-FR Notice

Summary of Deficiency Type(s)

[X] Agency Initiated [X] Registrant Initiated

Is "Fix" in-house? Yes

Describe Interactions with Company(Describe when Contacted and Company's Response including response to Previous Negotiated Due Dates:)

EPA spent a lot of time communicating with the applicant about deficiencies that needed to be addressed before completion of the comprehensive risk assessments. EPA had to send out four official correspondences (one 10-day deficiency letter, one response to a preliminary response to a 75-day deficiency letter, and two 75-day deficiency letters), and the time used to send and receive correspondence took up a large amount of the PRIA timeframe (about a year, as indicated by the dates below). The 10-day deficiency letter and first 75-day deficiency letter stated the applicant needed to submit a bridging study and additional genome sequencing information as the new active ingredient was isolated from a currently registered product and the applicant wanted to rely on toxicity and ecological data associated with the active ingredient in the currently registered product. After review of the bridging study, genome sequencing information, and the other data/information submitted by the applicant to support the initial applications, EPA issued a second 75-day deficiency letter that indicated a need for additional product chemistry data (e. g., analysis of contaminants post formulation, update to manufacturing process, and safety data sheets for starting materials). - 05/10/2017 - EPA issued a 10-day deficiency letter communicating deficiencies, including the need for a bridging study and additional genome sequencing information as the active ingredient was isolated from a currently registered product and the applicant wanted to rely on toxicity and ecological data associated with the active ingredient in the currently registered product. - 05/31/2017 - EPA received a 10-day deficiency letter response from the applicant stating it disagreed with EPA's determination that a bridging study and further genome sequencing information were needed. The applicant said that, if EPA had changed its technical position from a 2015 meeting, it wanted EPA to provide a detailed technical basis for the change. - 07/13/2017 - EPA sent a 75-day deficiency letter to the applicant explaining why the bridging study and genome sequencing information were needed. - 08/09/2017 - EPA received the applicant's preliminary response to the 75-day deficiency letter; the applicant again asked EPA to provide a detailed technical basis for its request for a bridging study (even though this was done in the 75-day deficiency letter). - 09/08/2017 - EPA responded to the applicant's preliminary 75-day deficiency letter response with its detailed technical basis for requesting the bridging study. - 09/26/2017 - EPA received the applicant's official response to the 75-day deficiency letter stating it would conduct a bridging study and additional genome sequencing. - 01/18/2018 - EPA received the bridging study and genome sequencing information from the applicant. - 03/09/2018 - BPPD's Risk Assessment Branch completed its review of the bridging study, genome sequencing information, and additional data/information submitted with the initial applications and indicated that issues were still remaining. - 04/04/2018 - EPA issued a second 75-day deficiency letter. - 06/18/2018 - EPA received the applicant's response to the second 75-day deficiency letter. - 07/18/2018 - EPA contacted the agent about negotiating the PRIA due date (12/18/2018 was proposed). - 07/24/2018 - After going back and forth on the new PRIA due date, the applicant agreed to a negotiated PRIA due date of 11/08/2018.

"75 Date" Letter Sent?	Yes
Date Sent	2018-04-04
Registrant Notified that this is the Last Negotiation?	NA

Rationale for Proposed Due Date: EPA needs to negotiate the PRIA due date from 08/02/2018 to 11/08 /2018 (approximately 3 months) to allow the following to be accomplished: - Complete the final comprehensive risk assessments - Complete the draft registration documents (proposed decision document, tolerance exemption, and supporting document for the tolerance exemption) based on completed risk assessments - Complete other associated reviews (e.g., of the labels) - Complete public participation process - Complete final decision document, publish tolerance exemption in the Federal Register, and issue registrations
Issue(s) Describe in Detail: See above in "Describe Interactions with Company" section.
Comment(s):

Approved /Disapproved:	Approved
Date of Final Decision	Mon Jul 30 16:41:54 EDT 2018 Richard Keigwin (RKEIGWIN) from IO (Host IP Address: 161.80.156.64)

e-Signature:
Richard Keigwin (RKEIGWIN) from IO (Host IP Address: 161.80.156.64)

Boukedes, Alexandra

From: Keeva Shultz <keeva@wagnerreg.com>
Sent: Tuesday, July 24, 2018 9:29 AM
To: Boukedes, Alexandra
Cc: Kausch, Jeannine; James Wagner; Anna Armstrong
Subject: RE: Bacillus amyloliquefaciens strain ENV503 (87645-G, 87645-U, and 7F8546) Renegotiated PRIA Date

Hi Alex,

Envera has agreed to the PRIA extension date of Nov. 8th, 2018.

Thank you,
Keeva Shultz

Wagner Regulatory Associates, Inc.
7217 Lancaster Pike, Suite A
Hockessin, DE 19707
302-635-7281
keeva@wagnerreg.com

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From: Boukedes, Alexandra [mailto:boukedes.alexandra@epa.gov]
Sent: Monday, July 23, 2018 2:29 PM
To: Keeva Shultz
Cc: Kausch, Jeannine; James Wagner; Anna Armstrong
Subject: RE: Bacillus amyloliquefaciens strain ENV503 (87645-G, 87645-U, and 7F8546) Renegotiated PRIA Date

Hi Keeva,

I am following up on the conversation we had on the phone earlier today. As discussed, a renegotiated PRIA date of September 2, 2018 or October 2, 2018 will not allow enough time to complete the remaining steps of the registrations process. After review of the April 4, 2018 75-day letter response and completion of the comprehensive science reviews, we need time to prepare the registration documents (e.g. decision document, tolerance exemption, and supporting document for the tolerance exemption), put them through review with management and our attorneys, put the reviewed documents and other relevant documents up for a public comment period, and then publish the final registration documents. To complete these steps we have to work with individuals internal and external to OPP and it takes time for these documents to move through the process.

We are proposing a new renegotiated PRIA date of November 8, 2018.

Please let me know if you have any questions or are interested in discussing this further over the phone.

Thanks,
Alex

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-347-0305
boukedes.alexandra@epa.gov

From: Keeva Shultz [mailto:keeva@wagnerreg.com]
Sent: Friday, July 20, 2018 12:49 PM
To: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Cc: Kausch, Jeannine <Kausch.Jeannine@epa.gov>; James Wagner <jmw@wagnerreg.com>; Anna Armstrong <Anna@wagnerreg.com>
Subject: RE: Bacillus amyloliquefaciens strain ENV503 (87645-G, 87645-U, and 7F8546) Renegotiated PRIA Date

Hi Alex,

After speaking with Envera this morning, it has been made clear that the September is the beginning of the Agricultural Companies planning cycle. This is a crucial month for many businesses, including Envera. We understand the agency needs more time to review the deficiency letters and other data submitted. Envera would respectfully ask for a 30 day renegotiation of the PRIA date (August 2, 2018) but would accept a 60 day renegotiation.

Thank you,
Keeva Shultz

Wagner Regulatory Associates, Inc.
7217 Lancaster Pike, Suite A
Hockessin, DE 19707
302-635-7281
keeva@wagnerreg.com

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From: Boukedes, Alexandra [mailto:boukedes.alexandra@epa.gov]
Sent: Thursday, July 19, 2018 7:53 AM
To: Keeva Shultz
Cc: Kausch, Jeannine
Subject: RE: Bacillus amyloliquefaciens strain ENV503 (87645-G, 87645-U, and 7F8546) Renegotiated PRIA Date

Hi Keeva,

Thank you for your confirmation of receipt. If you have any questions, please let me know.

Thanks,
Alex

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-347-0305
boukedes.alexandra@epa.gov

From: Keeva Shultz [mailto:keeva@wagnerreg.com]
Sent: Thursday, July 19, 2018 7:23 AM
To: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Cc: Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: RE: Bacillus amyloliquefaciens strain ENV503 (87645-G, 87645-U, and 7F8546) Renegotiated PRIA Date

Hi Alex,

This has been received. I will talk to my client and get back to you.

Thank you,
Keeva Shultz

Wagner Regulatory Associates, Inc.
7217 Lancaster Pike, Suite A
Hockessin, DE 19707
302-635-7281
keeva@wagnerreg.com

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From: Boukedes, Alexandra [mailto:boukedes.alexandra@epa.gov]
Sent: Wednesday, July 18, 2018 4:38 PM
To: Keeva Shultz

Cc: Kausch, Jeannine
Subject: Bacillus amyloliquefaciens strain ENV503 (87645-G, 87645-U, and 7F8546) Renegotiated PRIA Date

Hi Keeva,

The current PRIA due date for the *Bacillus amyloliquefaciens* strain ENV503 applications (87645-G, 87645-U, and 7F8546) is August 2, 2018. Although we have been diligently working on the *Bacillus amyloliquefaciens* strain ENV503 applications, we have unfortunately encountered several significant time delays (e.g., issuance of two 75-day deficiency letters on July 13, 2017, and April 4, 2018; issuance of a response to a rebuttal from you regarding our request to conduct a bridging acute IV toxicity/pathogenicity study on September 8, 2017; and awaiting your responses to our deficiency correspondence). We will therefore not be able to complete all of the remaining required actions for these applications prior to the current PRIA due date, which include, among other things, review of the response to the April 4, 2018, 75-day deficiency letter, public participation, and publication of the tolerance exemption in Federal Register. Given the remaining work to be completed on our end and the time that has been dedicated to ensuring that key deficiencies are addressed, we would respectfully propose a new PRIA due date of December 18, 2018, for the *Bacillus amyloliquefaciens* strain ENV503 applications.

We would like to move forward with negotiation paperwork for these applications no later than early next week and would need your agreement before doing so; a response to this email, citing the specific aforementioned applications, will suffice. Please let me know if you have any questions or concerns.

Thanks,
Alex

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
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boukedes.alexandra@epa.gov

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: **February 26, 2018**

SUBJECT: Review of Product Chemistry and Manufacturing Processes for ENV503 Biofungicide MUP and ENV503 Biofungicide Wettable Powder containing a New Active Ingredient *Bacillus amyloliquefaciens* strain ENV503 (PC Code 129287) - (Decision Nos: 526002, 526004; DP Barcode Nos: 438484, 438486; Submission #s: 998073, 998083; MRID Nos: 50159804, 50159902).

FROM: Mohammed Zuber, Ph.D., Biologist
Risk Assessment Branch (RAB)
Biopesticides & Pollution Prevention Division (7511P)

THROUGH: John Kough, Ph.D., Senior Scientist
Risk Assessment Branch (RAB)
Biopesticides & Pollution Prevention Division (7511P)

TO: Alexandra Boukedes, Regulatory Action Leader,
Microbial Pesticides Branch (MPB)
Biopesticides & Pollution Prevention Division (7511P)

ACTION REQUESTED: To review Product Chemistry and Manufacturing Processes for ENV503 Biofungicide MUP and ENV503 Biofungicide Wettable Powder containing a New Active Ingredient *Bacillus amyloliquefaciens* strain ENV503 (PC Code 129287)

CONCLUSIONS:

ENV503 Biofungicide MUP: Product Identity, Manufacturing Process, Discussion of Formation of Unintentional Ingredients, Analysis of Samples, Certification of Limits, and Physical and Chemical Properties (MRID: 50159804) – UNACCEPTABLE, but UPGRADEABLE to ACCEPTABLE subject to satisfactory submission of data on Microbial Contaminant Analysis of the five test batches of the MUP

ENV503 Biofungicide Wettable Powder: Product Identity, Manufacturing Process, Discussion of Formation of Unintentional Ingredients, Analysis of Samples, Certification of Limits, and Physical and Chemical Properties (MRID: 50159902) - SUPPLEMENTAL

DATA EVALUATION RECORD:

Active Ingredient: *Bacillus amyloliquefaciens* strain ENV503 (PC Code 129287)
Manufacturing Use Product (MUP): ENV503 Biofungicide MUP
End Use Product (EP): ENV503 Biofungicide Wettable Powder
Company Name: Envera, LLC
DP Barcode Nos.: 438484, 438486
MRID Nos.: 50159804, 50159902

Background:

ENV503 Biofungicide MUP is a manufacturing-use product (MUP) used in the manufacture of the end use product (EP) ENV503 Biofungicide Wettable Powder. The EP will be used as a broad spectrum biological fungicide on all field grown food crops including vegetables, herbs, small fruits, berries, fruit and nut trees, and in greenhouse production and hydroponics. The registrant is seeking registration for this MUP along with the EP. The active ingredient contained in the MUP and EP is *Bacillus amyloliquefaciens* strain ENV503 with a minimum concentration of 5.5×10^{10} CFU/g (1.30%, w/w) and 6.33×10^{9} CFU/g (0.15%, w/w), respectively. The EP is used as a foliar spray or soil drench in combination with and/or rotation with chemical fungicides for the prevention, control and suppression of many soil borne and foliar diseases. The EP is most effective when applied prior to the onset of disease. The active ingredient produces broad-spectrum antibiotic (lutrin) lipopeptides that disrupt pathogen cell wall formation. It is a competitive and fast colonizing bacterium, occupies plant's root hairs and leaves, and prevents the growth of soil borne and foliar pathogens by inducing systemic resistance in plants.

Bacillus amyloliquefaciens strain ENV503 was isolated from a commercially available Companion product. The Registrant demonstrated by nucleotide sequence analysis that *Bacillus amyloliquefaciens* strain ENV503 is identical to *Bacillus subtilis* strain GB03 (PC Code: 129068), whose nomenclature was later changed to *Bacillus amyloliquefaciens*. Strain GB03 was previously registered by the Agency (EPA Reg. No.: 7501-144). The Registrant is seeking to register strain ENV503 as a new active ingredient.

SUMMARY OF DATA SUBMITTED:

Study Types: Product Identity, Manufacturing Process, Discussion of Formation of Unintentional Ingredients, Analysis of Samples, Certification of Limits, and Physical and Chemical Properties

OCSPP Guidelines: 885.1100, 885.1200, 885.1300, 885.1400, 885.1500, 830.6302, 830.6303, 830.6304, 830.6313, 830.6317, 830.6319, 830.6320, 830.7000, 830.7100, 830.7300

Test Material: ENV503 Biofungicide MUP

MRID: 50159804

Discussion: The active ingredient contained in this MUP is *Bacillus amyloliquefaciens* strain ENV503 (1.30%, w/w) with a minimum concentration of 5.5×10^{10} CFU/g. The CSF and label for this MUP are in agreement concerning the amount of active ingredient. The remaining contents of this MUP are composed of inert ingredients. Adequate description of the characterization of *Bacillus amyloliquefaciens* strain ENV503 was provided. The description of the manufacturing process is acceptable, except that MSDSs for the starting materials were not provided. The formation of potential impurities was adequately discussed. An acceptable analysis of samples was provided and no data for contaminant and pathogen screenings were provided. The certified limits for the active ingredient and inert ingredient are within their respective OCSPP-recommended ranges. An acceptable description of the enforcement analytical method was submitted. The physical/chemical properties of the product were adequately addressed, with the exception that no experimental details were provided for the determination of stability to normal and elevated temperatures/metals/metal ions, pH and density. The registrant agrees to conduct one-year storage stability and corrosion characteristics studies as a condition of registration. Results for both studies must be submitted upon completion.

Deficiency: The Registrant demonstrated by nucleotide sequence analysis that *Bacillus amyloliquefaciens* strain ENV503 is identical to *Bacillus subtilis* strain GB03 (PC Code: 129068), whose nomenclature was later changed to *Bacillus amyloliquefaciens*. Strain GB03 was previously registered by the Agency (EPA Reg. No.: 7501-144). The Registrant is seeking to register strain ENV503 as a new active ingredient.

Classification: The product identity and chemistry studies are classified as UNACCEPTABLE, but UPGRADEABLE to ACCEPTABLE subject to satisfactory submission of data on Microbial Contaminant Analysis of the five test batches of the MUP. The studies were conducted in accordance with the recommendations for product identity and chemistry. No contaminants besides Gram-Negative bacteria were analyzed as part of the five-batch analysis. No data for pathogen screening was provided. No experimental procedures were provided for determining these physical-chemical properties: stability to normal and elevated temperatures/metals/metal ions, pH and density.

Study Types: Product Identity, Manufacturing Process, Discussion of Formation of Unintentional Ingredients, Analysis of Samples, Certification of Limits, and Physical and Chemical Properties

OCSPP Guidelines: 885.1100, 885.1200, 885.1300, 885.1400, 885.1500, 830.6302, 830.6303, 830.6304, 830.6313, 830.6317, 830.6319, 830.6320, 830.7000, 830.7100, 830.7300

Test Material: ENV503 Biofungicide Wettable Powder

MRID: 50159902

Discussion: ENV503 Biofungicide Wettable Powder is an end use product (EP) that contains the microbial active ingredient *Bacillus amyloliquefaciens* strain ENV503 (0.15%, w/w) at a minimum concentration of 6.33×10^9 CFU/g. The CSF and product label are in agreement with regard to the active ingredient concentration. Acceptable discussion of the formation of unintentional ingredients was submitted. An analysis of samples for ENV503 Biofungicide Wettable Powder would not be required if the TGAI/MUP becomes registered. The certified limits for the ingredients given on the CSF are within their respective OCSPP-recommended ranges. The description of the enforcement analytical method is acceptable. The physical/chemical properties of the product were adequately addressed, with the exception that no data was submitted for pH, and no experimental details were provided for the determination of density and stability to normal and elevated temperatures/metals/metal ions. The registrant agrees to conduct one-year storage stability and corrosion characteristics studies as a condition of registration. Results for both studies must be submitted upon completion.

Deficiency: The Registrant demonstrated by nucleotide sequence analysis that *Bacillus amyloliquefaciens* strain ENV503 is identical to *Bacillus subtilis* strain GB03 (PC Code: 129068), whose nomenclature was later changed to *Bacillus amyloliquefaciens*. Strain GB03 was previously registered by the Agency (EPA Reg. No.: 7501-144). The Registrant is seeking to register strain ENV503 as a new active ingredient.

Classification: The product identity and chemistry studies are classified as supplemental. The studies were conducted in accordance with the recommendations for product identity and chemistry. No experimental procedures were provided for determining these physical-chemical properties: stability to normal and elevated temperatures/metals/metal ions and density. No data was submitted for pH.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

DATE: **March 9, 2018**

SUBJECT: *Bacillus amyloliquefaciens* strain ENV503 (PC Code 129287) – Human Health Assessment Summary (Decision Nos: 526002, 526004, 526005; DP Barcode Nos: 438484, 438486, 438497, 445238; Submission #s: 998073, 998083, 998077, 1009410; MRID Nos: 50159801 - 04, 50159901 – 02, 50503801).

FROM: Mohammed Zuber, Ph.D., Biologist
Risk Assessment Branch (RAB)
Biopesticides & Pollution Prevention Division (7511P)

THROUGH: John Kough, Ph.D., Senior Scientist
Risk Assessment Branch (RAB)
Biopesticides & Pollution Prevention Division (7511P)

TO: Alexandra Boukedes, Regulatory Action Leader,
Microbial Pesticides Branch (MPB)
Biopesticides & Pollution Prevention Division (7511P)

Background:

ENV503 Biofungicide MUP (EPA Reg. No.: 87645-G; Company: ENVERA, LLC) is a proposed manufacturing-use product (MUP) to be used in the manufacture of the end use product (EP) ENV503 Biofungicide Wettable Powder (EPA Reg. No.: 87645-U). ENV503 Biofungicide Wettable Powder contains the active ingredient *Bacillus amyloliquefaciens* ENV503 which is a naturally occurring (Non-GMO) rhizosphere bacterium and plant growth promoting rhizobacterium (PGPR) that quickly establishes beneficial colonies on the plant's roots and leaves. It protects the roots from invading pathogens, stimulates healthier roots and improves nutrient uptake. *Bacillus amyloliquefaciens* ENV503 triggers the plant's natural immune system referred to as Induced Systemic Resistance (ISR). The EP will be used as a broad spectrum biological fungicide on all field grown food crops including vegetables, herbs, small fruits, berries, fruit and nut trees, and in greenhouse and hydroponic production. The EP will be used as a foliar/soil spray (in-furrow, banding and sprinkler systems), irrigation or soil/root drench alone or in combination or rotation with chemical fungicides. The EP is also being proposed for pre-plant seed treatment and commercial seed treatment applications. The EP is most effective when applied prior to the onset of the disease. It can also be applied up to and including

the day of harvest for all crops. The Registrant is seeking registration for this MUP along with the EP. The active ingredient contained in the MUP and EP is *Bacillus amyloliquefaciens* strain ENV503 with a minimum concentration of 5.5×10^{10} CFU/g (1.30%, w/w) and 6.33×10^{9} CFU/g (0.15%, w/w), respectively.

Bacillus amyloliquefaciens strain ENV503 was isolated from a commercially available product Companion Biofungicide. It was demonstrated by nucleotide sequence analysis that *Bacillus amyloliquefaciens* strain ENV503 is identical (Reference #1) to *Bacillus subtilis* strain GB03 (PC Code: 129068), whose nomenclature was later changed to *Bacillus amyloliquefaciens* strain GB03. Strain GB03 was previously registered by the Agency (EPA Reg. No.: 7501-144), however, the Registrant is seeking to register strain ENV503 as a new active ingredient.

Microbial Use Pattern:

The EP is a broad spectrum biological fungicide for the prevention, control and suppression of many soil borne and foliar diseases. It may be applied by foliar/soil spray (in-furrow, banding and sprinkler systems), irrigation or soil/root drench in combination or rotation with chemical fungicides on all field grown food crops including vegetables, herbs, small fruits, berries, fruit and nut trees, and in greenhouses and hydroponics. It can also be used for seed treatment as well as on grasses intended for seed, sod and forage. The EP is most effective when applied prior to the onset of the disease. It can also be applied up to and including the day of harvest for all crops.

The active ingredient produces broad-spectrum antibiotic (lutrin) lipopeptides that disrupt pathogen cell wall formation. It is a competitive and fast colonizing bacterium, occupies plant's root hairs and leaves, and prevents the growth of soil borne and foliar pathogens by inducing systemic resistance in plants.

MUP and EP Product Chemistry:

The microbial identification data reported in support of this active ingredient was satisfactory. The product chemistry studies for the MUP (MRID: 50159804) and EP (MRID: 50159902) are classified as "unacceptable" and "supplemental", respectively.

Human Health Assessment:

Toxicity, pathogenicity and infectivity data for the MUP and EP are summarized in Tables 1A and 1B.

Table 1A. Summary of Toxicity, pathogenicity and infectivity data for the MUP			
Data Requirement	OCSPP (OPPTS) Guideline No.	Results Summary, Classification and Toxicity Category	MRID No.

Table 1A. Summary of Toxicity, pathogenicity and infectivity data for the MUP			
Data Requirement	**OCSPP (OPPTS) Guideline No.**	**Results Summary, Classification and Toxicity Category**	**MRID No.**
Acute Oral Toxicity/Pathogenicity	885.3050	Registrant requested for waiver using acute oral toxicity (OCSPP 870.1100) results for the MUP (EPA Toxicity Category IV; MRID: 50159801). No data on the microbial clearance was reported in this study. However, the Registrant demonstrated microbial clearance in an acute injection toxicity/pathogenicity study (MRID: 50503801). **Classification: Acceptable**	50159803
Acute Inhalation Toxicity	870.1300	Testing waived based on (1) results from an acute pulmonary toxicity/pathogenicity study (OCSPP 885.3150) conducted with *Bacillus subtilis* strain GB03 (MRID: 41812304) demonstrating that strain GB03 was not infectious, pathogenic or toxic to rats when administered intratracheally, and (2) the MUP inerts are not expected to be toxic by the inhalation route, and the predominant inert has a demonstrated acute inhalation LC50 > 4.74 mg/L. **Toxicity Category: IV** **Classification: Acceptable**	50159803
Acute Pulmonary Toxicity/Pathogenicity	885.3150	Testing waived based on (1) Guideline 885.3150 study results (not infectious, pathogenic or toxic: MRID: 41812304) for the strain GB03 (EPA Reg. No.: 7501-144), and (2) nucleotide sequence results demonstrating that strains ENV503 and GB03 are identical. **Classification: Acceptable**	50159803
Acute Injection Toxicity/Pathogenicity	885.3200	MUP was determined to be non-toxic to rats when injected intravenously at a dose of 2.5×10^8 CFU/ml or 2.5×10^7 CFU/rat. A steady diminishment of viable CFU counts was demonstrated in all the organs tested with bacterial counts at, near or below the limits of detection on Day 42, the last day of this Study. **Classification: Acceptable**	50503801
Acute Oral Toxicity	870.1100	Results of the acute oral toxicity study showed no mortality after a single oral dose of 5,000 mg/kg of the MUP in female rats. **Toxicity Category: IV** **Classification: Acceptable**	50159801

Table 1A. Summary of Toxicity, pathogenicity and infectivity data for the MUP			
Data Requirement	**OCSPP (OPPTS) Guideline No.**	**Results Summary, Classification and Toxicity Category**	**MRID No.**
Acute Dermal Toxicity	870.1200	Testing waived based on (1) dermal toxicity results (Non-toxic; EPA Toxicity Category IV; MRID: 41812303) for the strain GB03 (EPA Reg. No.: 7501-144), and (2) nucleotide sequence results demonstrating that strains ENV503 and GB03 are identical. **Toxicity Category: IV** **Classification: Acceptable**	50159803
Acute Eye Irritation	870.2400	A single application of MUP ($5.8x10^9$ CFU) when instilled into the conjunctival sac of the right eye in rabbits (two female and one male) was minimally irritating. **Toxicity Category: IV** **Classification: Acceptable**	50159802
Acute Dermal Irritation	870.2500	Testing waived based on (1) dermal toxicity results (Non-Toxic; EPA Toxicity Category IV; MRID: 41812303) for the strain GB03 (EPA Reg. No.: 7501-144), and (2) nucleotide sequence results demonstrating that strains ENV503 and GB03 are identical. **Toxicity Category: IV** **Classification: Acceptable**	50159803
Hypersensitivity Incidents	885.3400	The applicant reported that no hypersensitivity incidents were observed among employees. Any future hypersensitivity incidents must be reported to the EPA (refer to test note #3 of 40 CFR § 158.2140(d)). **Classification: Acceptable**	50159803
Cell Culture	885.3500	Not required because the active ingredient is not a virus (refer to test note #4 of 40 CFR § 158.2140(d)). **Classification: Acceptable**	50159803

Table 1B. Summary of Toxicity, pathogenicity and infectivity data for the EP			
Data Requirement	**OCSPP (OPPTS) Guideline No.**	**Results Summary, Classification and Toxicity Category**	**MRID No.**

Table 1B. Summary of Toxicity, pathogenicity and infectivity data for the EP			
Data Requirement	**OCSPP (OPPTS) Guideline No.**	**Results Summary, Classification and Toxicity Category**	**MRID No.**
Acute Inhalation Toxicity	870.1300	Testing waived based on (1) results from an acute pulmonary toxicity/pathogenicity study (OCSPP 885.3150) conducted with *Bacillus subtilis* strain GB03 (MRID: 41812304) demonstrating that strain GB03 was not infectious, pathogenic or toxic to rats when administered intratracheally, and (2) the EP inerts are not expected to be toxic by the inhalation route, and the predominant inert has a demonstrated acute inhalation LC50 > 4.74 mg/L. **Toxicity Category: IV** **Classification: Acceptable**	50159901
Acute Oral Toxicity	870.1100	Testing waived based on the results (No Mortality) from an acute oral toxicity study (OCSPP 870.1100) demonstrating classification of ENV503 Biofungicide MUP as EPA Toxicity Category IV (MRID: 50159801). **Toxicity Category: IV** **Classification: Acceptable**	50159901
Acute Dermal Toxicity	870.1200	Testing waived based on (1) dermal toxicity results (Non-Toxic; EPA Toxicity Category IV; MRID: 41812303) for the strain GB03 (EPA Reg. No.: 7501-144), and (2) nucleotide sequence results demonstrating that strains ENV503 and GB03 are identical. **Toxicity Category: IV** **Classification: Acceptable**	50159901
Acute Eye Irritation	870.2400	Testing waived based on the results for the MUP (MRID: 50159802) showing that a single application of MUP (5.8×10^9 CFU) when instilled into the conjunctival sac of the right eye in rabbits (two female and one male) was minimally irritating. **Toxicity Category: IV** **Classification: Acceptable**	50159901
Acute Dermal Irritation	870.2500	Testing waived based on (1) dermal toxicity results (Non-Toxic; EPA Toxicity Category IV; MRID: 41812303) for the strain GB03 (EPA Reg. No.: 7501-144), and (2) nucleotide sequence results demonstrating that strains ENV503 and GB03 are identical. **Toxicity Category: IV** **Classification: Acceptable**	50159901

Dietary Exposure and Risk Characterization:

Bacillus amyloliquefaciens strain ENV503 is proposed to be used as a foliar/soil spray (in-furrow, banding and sprinkler systems), irrigation or soil/root drench in combination or rotation with chemical fungicides on all field grown food crops including vegetables, herbs, small fruits, berries, fruit and nut trees, and in greenhouses and hydroponics. It can also be used for seed treatment as well as on grasses intended for seed, sod and forage. The EP is most effective when applied prior to the onset of the disease. It can also be applied up to and including the day of harvest for all crops. Therefore, dietary exposure to this active ingredient is expected. However, *Bacillus amyloliquefaciens* strain ENV503 is not anticipated to be a dietary concern as residues of the bacterial spore are not taken up systemically in plants. Therefore, no pesticidal exposure to the bacterial spore is expected in raw agricultural commodities; hence, a qualitative dietary assessment was conducted. In addition, it has been demonstrated by nucleotide sequence analysis (MRID: 50159804) that strain ENV503 is identical to the previously registered active ingredient, strain GB03 (PC Code: 129068; EPA Reg. No.: 7501-144) for which the Agency has established a tolerance exemption (Petition #: 1F3968; 40 CFR 1111). Therefore, the Agency concludes that no risk is anticipated from dietary exposure to residues of the bacterial spore in raw agricultural commodities.

Occupational Exposure and Risk Characterization:

Based on the proposed use pattern, there is potential for occupational exposure to applicators and handlers through dermal and inhalation routes. However, based on the animal testing of *Bacillus amyloliquefaciens* strain ENV503, no toxicity, irritation, infectivity, pathogenicity or other adverse effects attributed to this microbial active ingredient and the end use product (EP) are expected. Therefore, a qualitative occupational assessment was conducted. The potential occupational exposure to *Bacillus amyloliquefaciens* strain ENV503 is not anticipated to exceed any toxicity thresholds, as long as pesticide handlers (e.g., applicators) follow the precautions identified on the EP label. The EP label requires pesticide handlers to wear a long-sleeved shirt, long pants, waterproof gloves, shoes, socks, protective eyewear and a respirator.

Residential and Non-Occupational Exposure and Risk Characterization:

ENV503 Biofungicide Wettable Powder is intended for agricultural/commercial use sites only. Therefore, no significant residential or non-occupational exposure from the use of this EP is anticipated. Planting of treated turf grass seed or sod in residential, commercial grounds areas could potentially result in non-occupational exposure to *Bacillus amyloliquefaciens* strain ENV503, however this exposure is not expected to be significant considering the ubiquitous presence of these microbes in the environment. Furthermore, as indicated above *Bacillus amyloliquefaciens* strain ENV503 is not toxic, irritating, pathogenic, or infective via the pulmonary route of exposure and is not irritating or toxic through the dermal route of exposure (Reference #2).

Aggregate Exposure and Risk Characterization:

In accordance with the Food Quality Protection Act (FQPA), OPP will typically consider and aggregate exposure and risk estimates from food, drinking water, residential uses of a pesticide, and other non-occupational sources of exposure. There are proposed turf (sod) use for *B. amyloliquefaciens* strain ENV503, however, a qualitative dietary assessment was conducted as no residues of the bacterial spore are anticipated in raw agricultural commodities. In addition, it has been demonstrated by nucleotide sequence analysis (MRID: 50159804) that strain ENV503 is identical to the previously registered active ingredient, strain GB03 (PC Code: 129068; EPA Reg. No.: 7501-144), for which the Agency has established a tolerance exemption (Petition #: 1F3968; 40 CFR 1111). Therefore, a quantitative aggregate assessment was not conducted for *B. amyloliquefaciens* strain ENV503.

Risk Characterization:

The Agency has considered human exposure to *B. amyloliquefaciens* strain ENV503 in light of the relevant safety factors in FQPA (FFDCA) and FIFRA. A determination has been made that no unreasonable adverse effects to the U.S. population in general, and to infants and children in particular, will result from the uses of *B. amyloliquefaciens* strain ENV503 as pesticides when label instructions are followed.

References:

1. Review of Product Chemistry and Manufacturing Processes for ENV503 Biofungicide MUP and ENV503 Biofungicide Wettable Powder containing a New Active Ingredient *Bacillus amyloliquefaciens* strain ENV503 (PC Code 129287) - (Decision Nos: 526002, 526004; DP Barcode Nos: 438484, 438486; Submission #s: 998073, 998083; MRID Nos: 50159804, 50159902). - Memo Dated March 9, 2018 from the Science Reviewer Mohammed Zuber to the Regulatory Action Leader Alexandra Boukedes.

2. Residential and Occupational Exposure Assessments: *Bacillus amyloliquefaciens* strain ENV503 (PC Code 129287) – Human Health Assessment Summary (Decision Nos: 526002, 526004, 526005; DP Barcode Nos: 438484, 438486, 438497, 445238; Submission #s: 998073, 998083, 998077, 1009410; MRID Nos: 50159801 - 04, 50159901 – 02, 50503801) – Memo Dated February 26, 2018 from the Acting Branch Chief of the Risk Assessment Branch Judy Facey to the Regulatory Action Leader of the Microbial Pesticides Branch Alexandra Boukedes.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

February 28, 2018

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

MEMORANDUM

SUBJECT: Environmental Risk Assessment for a FIFRA Section 3 Registration of two products, *Bacillus amyloliquefaciens* strain ENV503 Technical Manufacturing Use Product and ENV503 Biofungicide Wettable Powder End Use Product, Containing the New Active Ingredient *Bacillus amyloliquefaciens* strain ENV503; EPA File Symbols 87645-G and 87645-U; PC Code 129287; Decision Nos. 526002 and 526004; Submission Nos. 998073 and 998083; DP Barcodes: 438488 and 438489

FROM: Sarah Butler, Biologist
Risk Assessment Branch
Biopesticides and Pollution Prevention Division

THROUGH: Shannon Borges, Senior Scientist
Risk Assessment Branch
Biopesticides and Pollution Prevention Division

TO: Alexandra Boukedes, Regulatory Action Leader
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division

I. Introduction

Envera, LLC (hereafter "Envera") has submitted an application for a Section 3 registration of a technical product (*Bacillus amyloliquefaciens* strain ENV503 Technical; EPA File Symbol 87645-G) containing a new active ingredient *Bacillus amyloliquefaciens* strain ENV503. This bacterium was previously classified as *Bacillus subtilis* var. *amyloliquefaciens*, but has been re-classified as its own species because DNA from strains of *B. amyloliquefaciens* have consistently been found to share less than 25% homology with DNA from strains of *B. subtilis* (Priest, 1987). *Bacillus amyloliquefaciens* organisms are rod-shaped, gram-positive, non-pathogenic, aerobic bacteria which are ubiquitous in nature and have been recovered from water, soil, air and decomposing plant residue. *Bacillus amyloliquefaciens* acts as a fungicide against fungal plant pathogens through nutrient competition, site exclusion and colonization (MRID No. 50159804). Envera isolated this strain of *Bacillus amyloliquefaciens* from a culture of *Bacillus subtilis* strain GB03 (PC Code 129068) which they obtained from a bottle of a previously registered pesticide, Companion, EPA Reg. No. 71065-3 (MRID No. 50159804).

One end use product (EP) has been proposed containing this new active ingredient (ENV503 Biofungicide Wettable Powder, EPA File Symbol 87645-U). This EP will contain 0.15% *Bacillus amyloliquefaciens* strain ENV503, at a minimum viability of 5.5 x 10^{10} colony-forming units (cfu) per gram. This EP is proposed for control of diseases caused by various fungal species including: *Alternaria* spp., *Aspergillus* spp., *Botrytis cinerea*, *Colletotrichum* spp., *Didymella bryoniae*, *Erwinia carotovora*, *Erwinia tracheiphila*, *Golovinomyces cichoracearum*, *Fusarium oxysporum*, *Fusarium solani*, *Candidatus Liberibacter* spp., *Phytophthora* spp., *Plasmodiophora brassicae*, *Podosphaera xanthii*, *Pseudomonas syringae*, *Pythium* spp., *Rhizoctonia solani*, *Sclerospora gramincola*, *Sclerotinia minor*, *Uncinula necator*, *Xanthomonas campestris*, and *Xanthomonas axonpodis*. It is proposed for use on food, non-food, and forage crops including: berries, brassica vegetables, cucurbits, citrus, vine crops, herbs and spices, fruiting vegetables, leafy vegetables, legumes, bulb vegetables, root / tuber and corm vegetables, tropical / subtropical fruits, and grasses grown for seed, sod production, pasture and forage grasses. This product can be applied to crops as a foliar and soil drench application, as an in-furrow application, via banding, via drip irrigation, or as a seed treatment. The application rates for this product range from 0.1 ounces to 0.5 ounces per 100 lb. of seed for seed treatment applications, and from 0.5 lb. to 1.5 lb. per acre for all other application methods. As a result of the wide range of crops and application methods proposed for this EP, exposure of nontarget organisms to *Bacillus amyloliquefaciens* strain ENV503 is a possible result of the use of the EP containing this active ingredient

II. Evaluation of Nontarget Data Submitted to Support Registration

Because this active ingredient was directly isolated from an already registered product, Companion, Envera has requested that the EPA bridge from existing Tier I nontarget organism studies and rationale for strain GB03 to this new active ingredient, ENV503. The product chemistry submitted by Envera for *Bacillus amyloliquefaciens* strain ENV503 (MRID 50159804) demonstrates that this strain is identical to *Bacillus subtilis* strain GB03, and at the time of the writing of this assessment, the EPA is in the process of reviewing a bridging study conducted by Envera to further demonstrate similarity between these two fungi. If this study is determined to be acceptable, the studies and rationales submitted for GB03 will be sufficient to satisfy the Tier I nontarget organism data requirements for the active ingredient, *Bacillus amyloliquefaciens* strain ENV503, contained in the technical product and the EP, and further testing of nontarget organisms at higher tier levels will not be required.

Envera submitted rationale to address the avian inhalation data requirement, and cited to several previously reviewed studies and rationale which assessed potential risk to nontarget organisms from exposure to *Bacillus subtilis* strain GB03 to address all other data requirements. The EPA's previous review of these studies and rationales found them to be acceptable and concluded that adverse effects to nontarget organisms were not expected as a result of exposure to *Bacillus subtilis* strain GB03 (U.S. EPA 2010). The EPA reviewed these previously submitted studies and rationale, as well as the new rationale on avian inhalation, as part of the registration process for the technical product and EP containing *Bacillus amyloliquefaciens* strain ENV503, and it was determined that the information provided was sufficient to satisfy the nontarget organism data requirements for this new active ingredient. The labels for currently registered end use products containing *Bacillus subtilis* strain GB03 were also reviewed, and it was determined that

the uses and application rates were comparable to those on the proposed label for the end use product containing *Bacillus amyloliquefaciens* strain ENV503. In addition, the four registered strains of *Bacillus subtilis*, including strain GB03, have undergone registration review, and the EPA concluded that all microbial pesticide non-target organism data requirements were fulfilled. No data-call ins were issued during the registration review of *Bacillus subtilis* (U.S. EPA 2010).

III. Literature Search

BPPD conducted literature searches to assess potential effects to nontarget organisms that could result from proposed applications of the EP containing *Bacillus amyloliquefaciens* strain ENV503. These searches were conducted in February of 2018, and used the Web of Science database. Searches were conducted using the Web of Science Core Collection, the default database within the Web of Science system, and results were restricted to articles published from 2010 to the present, as the previously mentioned registration review of *Bacillus subtilis* reviewed any relevant articles published before 2010.

One search was conducted using the terms "*Bacillus amyloliquefaciens* and insects" which returned 18 results. Two of these results were examined further, as they evaluated the effects of rearing insect larvae on plant leaves inoculated with *Bacillus amyloliquefaciens*. One study showed reduced growth and higher mortality in fourth-instar larvae of fall armyworms (*Spodoptera fruigiperda*) fed with leaves of *Hosta* spp. treated with *Bacillus amyloliquefaciens* compared to control leaves (Li et al., 2015). However, observed mortality was only 30% among fall armyworms in this study. In a similar study, *Bacillus amyloliquefaciens* was applied to *Calabrese* spp. via drenching at a concentration of 10^8 cfu/mL, and 45 days later, *Brevicoryne brassicae* adults were introduced to the plants and allowed to feed, colonize and reproduce (Gadhave and Gange, 2016). It was determined that the growth rate of *B. brassicae* populations was significantly lower on treated plants compared to control plants, as were the final *Brevicoryne brassicae* population sizes. The researchers believed however, that these reductions resulted from effects of *B. amyloliquefaciens* on biochemical and nutritional qualities of the plants, and not necessarily from direct effects of the bacteria on the insects. These results do not change the conclusions previously made regarding potential risk to nontarget insects from exposure to the currently proposed EP. EPA has previously reviewed studies on the exposure of three insect species and honey bees to Companion (the currently registered EP containing *Bacillus subtilis* strain GB03), and concluded that no adverse effects were expected in nontarget insects as a result of exposure to *B. subtilis* strain GB03 (U.S. EPA 20010). Therefore, since the search results do not indicate effects warranting concern, and because EPA has insect data specific to the active ingredient, these search results do not raise any concerns.

Searches were also conducted using the terms "*Bacillus amyloliquefaciens* and avian", "*Bacillus amyloliquefaciens* and mammals", "*Bacillus amyloliquefaciens* and terrestrial plants", And "*Bacillus amyloliquefaciens* and aquatic organisms" which returned one, two, one, and zero results respectively. It was determined that none of these results were relevant, as they did not discuss potential effects of *Bacillus amyloliquefaciens* on birds, mammals, terrestrial plants, or aquatic organisms.

IV. Conclusion

The EPA has reviewed all relevant labels, memoranda, and registration review documents for *Bacillus subtilis* strain GB03, as well as relevant scientific literature on *Bacillus amyloliquefaciens* strain ENV503, and has determined that adverse effects to nontarget organisms resulting from proposed label applications of *Bacillus amyloliquefaciens* strain ENV503 are not expected. Since EPA has determined that no effects are anticipated for any non-target species exposed to *Bacillus amyloliquefaciens* strain ENV503 as a result of the proposed labeled applications, effects to federally listed threatened and endangered ('listed') species and their designated critical habitats are also not expected. Therefore, a "No Effect" determination is made for direct and indirect effects to listed species and their designated critical habitats resulting from the proposed uses of *Bacillus amyloliquefaciens* strain ENV503, as labeled.

V. References

Gadhave, KR, and Gange, AC. (2016). Plant-associated *Bacillus* spp. alter life-history traits of the specialist insect *Brevicoryne brassicae* L. Agricultural and Forest Entomology 18(1): 35-42.

Li, H, Soares, MA, Torres, MS, Bergen, M, and White Jr, JF. (2015), Endophytic bacterium, *Bacillus amyloliquefaciens*, enhances ornamental hosta resistance to diseases and insect pests. Journal of plant interactions 10(1): 224-229.

Priest, FG, Goodfellow, M, Shute, LA, & Berkeley, RCW. (1987). *Bacillus amyloliquefaciens* sp. nov., nom. rev. International Journal of Systematic and Evolutionary Microbiology 37(1): 69-71.

U.S. EPA. 2010. *Bacillus subtilis* final Reregistration Review decision. Case 6012. Docket No. EPA-HQ-OPP-2007-1026.

Submitted via EPA CDX PSP portal

WRA

Wagner Regulatory Associates, Inc.
P.O. Box 640
7460 Lancaster Pike, Suite 9
Hockessin, Delaware 19707

January 19, 2018

Document Processing Desk (REGFEE)
ATTN: Alexandra Boukedes, Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Dear Ms. Boukedes,

Re: ENV503 Biofungicide; EPA File Symbols 87645-G, 87645-U and PP #7F8546
Response to Agency letter of July 13, 2017

As agreed with the Agency, I am submitting the enclosed report for ENV503:

MRID 50503801: Doig, A., (2018), ENV503 Intravenous Toxicity/ Pathogenicity Study in Rats, OCSPP 885.3200, Stillmeadow, Inc., Study ID 21337-17, 45 pages.

Also enclosed is the data transmittal and a copy of the Agency's letter of 7/13/2017. Please contact me if you require any further information on this. Thank you.

Sincerely,

James M Wagner

James M. Wagner
Agent for Envera, LLC
Tel: (302) 635-7290
Email: jmw@wagnerreg.com

cc: Envera, LLC

DATA TRANSMITTAL DOCUMENT

1. **Name and Address of Submitter**
   Envera LLC
   c/o Wagner Regulatory Associates
   PO Box 640
   Hockessin, DE 19707

2. **Regulatory Action In Support Of Which This Package Is Submitted**
   ENV503 Biofungicide; 87645-U; 87645-G; PP#7F8546

3. **Transmittal Date**
   January 19, 2018

4. **List of Submitted Studies**

50503801	Doig, A., (2018), ENV503 Intravenous Toxicity/ Pathogenicity Study in Rats, OCSPP 885.3200, Stillmeadow, Inc., Study ID 21337-17, 45 pages.

Company Official: James M. Wagner, Agent
Name

Signature: James M. Wagner

Company Name: **Envera LLC**

Company Contact:

James M. Wagner — Name

(302) 635-7290 — Phone

spreadsheet contains a separate worksheet for each state covered by that program showing each unit preliminarily identified as eligible for a second-round NUSA allocation. Each state worksheet also contains a summary showing (1) the quantity of allowances initially available in that state's 2017 NUSA, (2) the sum of the 2017 NUSA allowance allocations that were made in the first round to new units in that state, if any, and (3) the quantity of allowances in the 2017 NUSA available for second-round allocations to new units (or ultimately for allocations to existing units), if any.

Objections should be strictly limited to whether EPA has correctly identified the units eligible for second-round 2017 NUSA allocations according to the criteria established in the regulations and should be emailed to the address identified in **ADDRESSES**. Objections must include: (1) Precise identification of the specific data the commenter believes are inaccurate, (2) new proposed data upon which the commenter believes EPA should rely instead, and (3) the reasons why EPA should rely on the commenter's proposed data and not the data referenced in this notice.

EPA notes that an allocation or lack of allocation of allowances to a given unit does not constitute a determination that CSAPR does or does not apply to the unit. EPA also notes that allocations are subject to potential correction if a unit to which NUSA allowances have been allocated for a given control period is not actually an affected unit as of the start of that control period.[2]

(Authority: 40 CFR 97.411(b), 97.511(b), 97.611(b), 97.711(b), and 97.811(b).)

Dated: December 1, 2017.

Reid P. Harvey,

Director, Clean Air Markets Division, Office of Atmospheric Programs, Office of Air and Radiation.

[FR Doc. 2017–27094 Filed 12–14–17; 8:45 am]

BILLING CODE 6560–50–P

[2] *See* 40 CFR 97.411(c), 97.511(c), 97.611(c), 97.711(c), and 97.811(c).

ENVIRONMENTAL PROTECTION AGENCY

[EPA–HQ–OPP–2017–0006; FRL–9970–50]

Receipt of Several Pesticide Petitions Filed for Residues of Pesticide Chemicals in or on Various Commodities

AGENCY: Environmental Protection Agency (EPA).

ACTION: Notice of filing of petitions and request for comment.

SUMMARY: This document announces the Agency's receipt of several initial filings of pesticide petitions requesting the establishment or modification of regulations for residues of pesticide chemicals in or on various commodities.

DATES: Comments must be received on or before January 16, 2018.

ADDRESSES: Submit your comments, identified by docket identification (ID) number and the pesticide petition number (PP) of interest as shown in the body of this document, by one of the following methods:

- *Federal eRulemaking Portal: http://www.regulations.gov.* Follow the online instructions for submitting comments. Do not submit electronically any information you consider to be Confidential Business Information (CBI) or other information whose disclosure is restricted by statute.
- *Mail:* OPP Docket, Environmental Protection Agency Docket Center (EPA/DC), (28221T), 1200 Pennsylvania Ave. NW, Washington, DC 20460–0001.
- *Hand Delivery:* To make special arrangements for hand delivery or delivery of boxed information, please follow the instructions at *http://www.epa.gov/dockets/contacts.html.*

Additional instructions on commenting or visiting the docket, along with more information about dockets generally, is available at *http://www.epa.gov/dockets.*

FOR FURTHER INFORMATION CONTACT: Robert McNally, Biopesticides and Pollution Prevention Division (7511P), main telephone number: (703) 305–7090; email address: *BPPDFRNotices@epa.gov.*, Michael Goodis, Registration Division (7505P), main telephone number: (703) 305–7090; email address: *RDFRNotices@epa.gov*, Steve Knizner, Antimicrobials Division (7510P), main telephone number: (703) 305–7090; email address: *ADFRNotices@epa.gov*, Michael Goodis. The mailing address for each contact person is: Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave. NW, Washington, DC 20460–0001.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

You may be potentially affected by this action if you are an agricultural producer, food manufacturer, or pesticide manufacturer. The following list of North American Industrial Classification System (NAICS) codes is not intended to be exhaustive, but rather provides a guide to help readers determine whether this document applies to them. Potentially affected entities may include:

- Crop production (NAICS code 111).
- Animal production (NAICS code 112).
- Food manufacturing (NAICS code 311).
- Pesticide manufacturing (NAICS code 32532).

If you have any questions regarding the applicability of this action to a particular entity, consult the person listed under **FOR FURTHER INFORMATION CONTACT** for the division listed at the end of the pesticide petition summary of interest.

B. What should I consider as I prepare my comments for EPA?

1. *Submitting CBI.* Do not submit this information to EPA through regulations.gov or email. Clearly mark the part or all of the information that you claim to be CBI. For CBI information in a disk or CD–ROM that you mail to EPA, mark the outside of the disk or CD–ROM as CBI and then identify electronically within the disk or CD–ROM the specific information that is claimed as CBI. In addition to one complete version of the comment that includes information claimed as CBI, a copy of the comment that does not contain the information claimed as CBI must be submitted for inclusion in the public docket. Information so marked will not be disclosed except in accordance with procedures set forth in 40 CFR part 2.

2. *Tips for preparing your comments.* When preparing and submitting your comments, see the commenting tips at *http://www.epa.gov/dockets/comments.html.*

3. *Environmental justice.* EPA seeks to achieve environmental justice, the fair treatment and meaningful involvement of any group, including minority and/or low-income populations, in the development, implementation, and enforcement of environmental laws, regulations, and policies. To help address potential environmental justice issues, the Agency seeks information on any groups or segments of the population who, as a result of their location, cultural practices, or other factors, may have atypical or disproportionately high and adverse human health impacts or environmental effects from exposure to the pesticides discussed in this document, compared to the general population.

II. What action is the Agency taking?

EPA is announcing its receipt of several pesticide petitions filed under section 408 of the Federal Food, Drug,

and Cosmetic Act (FFDCA), 21 U.S.C. 346a, requesting the establishment or modification of regulations in 40 CFR part 180 for residues of pesticide chemicals in or on various food commodities. The Agency is taking public comment on the requests before responding to the petitioners. EPA is not proposing any particular action at this time. EPA has determined that the pesticide petitions described in this document contain the data or information prescribed in FFDCA section 408(d)(2), 21 U.S.C. 346a(d)(2); however, EPA has not fully evaluated the sufficiency of the submitted data at this time or whether the data support granting of the pesticide petitions. After considering the public comments, EPA intends to evaluate whether and what action may be warranted. Additional data may be needed before EPA can make a final determination on these pesticide petitions.

Pursuant to 40 CFR 180.7(f), a summary of each of the petitions that are the subject of this document, prepared by the petitioner, is included in a docket EPA has created for each rulemaking. The docket for each of the petitions is available at *http://www.regulations.gov*.

As specified in FFDCA section 408(d)(3), 21 U.S.C. 346a(d)(3), EPA is publishing notice of the petition so that the public has an opportunity to comment on this request for the establishment or modification of regulations for residues of pesticides in or on food commodities. Further information on the petition may be obtained through the petition summary referenced in this unit.

III. Amended Tolerance Exemptions for Non-Inerts (Except PIPS)

1. *PP 7F8547*. (EPA–HQ–OPP–2017–0526). Bayer CropScience LP, 2 T.W. Alexander Dr., Research Triangle Park, NC 27709, requests to amend an exemption from the requirement of a tolerance in 40 CFR 180.1257 for residues of the nematocide Purpureocillium lilacinum (synonym Paecilomyces lilacinus) strain 251 in or on all agricultural commodities to update the taxonomic description. The petitioner believes no analytical method is needed because the active ingredient has only been renamed and remains unchanged. *Contact:* BPPD.

IV. Amended Tolerances for Non-Inerts

1. *PP 7E8597*. (EPA–HQ–OPP–2017–0476). Interregional Research Project No. 4 (IR–4), Rutgers, The State University of New Jersey, 500 College Road East, Suite 201 W, Princeton, NJ 08540, requests that the existing tolerance in 40 CFR 180.355(a) General. (1) for the combined residues of the herbicide bentazon (3-isopropyl-1*H*-2,1,3-benzothiadiazin-4(3*H*)-one-2,2-dioxide) and its 6- and 8-hydroxy metabolites in or on pea, dry, seed be increased from 1.0 ppm to 3.0 ppm. Upon establishment of the amended tolerance, the Petitioner requests that the previously established tolerance for bentazon on pea, dry, seed at 1.0 ppm is removed. Adequate enforcement methodolog (gas liquid chromatography (GLC) methods are available for the determination of residues of bentazon and its 6- and 8-hydroxy metabolites in/on plant commodities. The limit of detection is 0.05 ppm for each regulated compound. *Contact:* RD

2. *PP 7F8592*. EPA–HQ–OPP–2017–0536. Syngenta Crop Protection, LLC 410 Swing Road, Greensboro, NC 27409, requests to amend the tolerance in 40 CFR part 180 for residues of the fungicide fludioxonil in or on Sugar beet at 5.0 parts per million (ppm). The method Syngenta Crop Protection Method AG–597B was used and has passed an Agency petition method validation for several commodities, and is currently the enforcement method to measure and evaluate the chemical fludioxonil. *Contact:* RD.

V. New Tolerance Exemptions for Inerts (Except Pips)

1. *PP IN–11063*. (EPA–HQ–OPP–2017–0474). Toxcel, LLC, on behalf of Lanxess Corporation, 111 RIDC Park West Drive, Pittsburgh, PA 15275, requests to establish an exemption from the requirement of a tolerance for residues of aspartic acid, N-(1,2-dicarboxyethyl)-, tetrasodium salt (CAS Reg. No. 144538–83–0) when used as an inert ingredient in antimicrobial pesticide formulations (food-contact surface sanitizing solutions) under 40 CFR 180.940(a). The petitioner believes no analytical method is needed because it is not required for an exemption from the requirement of a tolerance. *Contact:* RD

2. *PP IN–11066*. (EPA–HQ–OPP–2017–0541). SciReg, Inc., 12733 Director's Loop, Woodbridge, VA 22192 on behalf of Solvay USA Inc., requests to establish an exemption from the requirement of a tolerance for residues of 2-isobutyl-2-methyl-1,3-dioxolane-4-methanol (CAS Reg. No. 5660–53–7) when used as an inert ingredient (solvent/cosolvent) in pesticide formulations applied to growing crops and raw agricultural commodities after harvest under 40 CFR 180.910and when used as an inert ingredient in antimicrobial pesticide formulations (food-contact surface sanitizing solutions) under 40 CFR 180.940(a). The petitioner believes no analytical method is needed because it is not required for an exemption from the requirement of a tolerance. *Contact:* RD.

VI. New Tolerance Exemptions for Non-Inerts (Except Pips)

1. *PP 7E8567*. (EPA–HQ–OPP–2017–0525). Interregional Research Project Number 4 (IR–4), Rutgers, The State University of New Jersey, 500 College Rd. East, Suite 201 W, Princeton, NJ 08540, requests to establish an exemption from the requirement of a tolerance in 40 CFR part 180 for residues of the microbial pesticide Pepino mosaic virus, strain CH2, isolate 1906 in or on tomato. The petitioner believes no analytical method is needed because Pepino mosaic virus, strain CH2, isolate 1906 is a naturally occurring, low risk plant virus that is not related to any animal or human pathogen and is not known to be able to survive in animal or human tissue. *Contact:* BPPD.

2. *PP 4F8325*. (EPA–HQ–OPP–2017–0063). ICA Trinova, Inc., 1 Beavers Street, Suite B, Newnan, GA 30263, requests to establish an exemption from the requirement of a tolerance for residues of the antimicrobial, sodium chlorite, in or on tomatoes. The petitioner believes no analytical method is needed because no residues of chlorate were detected in tomato puree from tomatoes treated post-harvest with gaseous chlorine dioxide generated from sodium chlorite. *Contact:* AD.

3. *PP 7F8546*. (EPA–HQ–OPP–2017–0460). Envera, LLC, 220 Garfield Ave., West Chester, PA 19380, requests to establish an exemption from the requirement of a tolerance in 40 CFR part 180 for residues of the bactericide and fungicide Bacillus amyloliquefaciens strain ENV503 in or on all food commodities. The petitioner believes no analytical method is needed because an exemption from the requirement of a tolerance is being proposed. *Contact:* BPPD.

4. *PP 7F8599*. (EPA–HQ–OPP–2017–0487). Suntton International Inc., 901 H St., Suite 610, Sacramento, CA 95814, requests to establish an exemption from the requirement of a tolerance in 40 CFR part 180 for residues of the plant regulator 24-epibrassinolide in or on all agricultural commodities. The petitioner believes no analytical method is needed because it is expected that, when used as proposed, 24-epibrassinolide would not result in residues that are of toxicological concern. *Contact:* BPPD.

VII. New Tolerances for Non-Inerts

1. *PP 7E8609* (EPA–HQ–OPP–2017–0532) OAT Agrio. Ltd. 1–3–1 Kanda Ogawa-machi, Chiyoda-ku Tokyo 101–0052, Japan c/o Landis International R&D Management 3185 Madison Highway, P.O. Box 5126, Valdosta, Georgia, 31603–5126, requests to establish a tolerance in 40 CFR part 180 for residues of the miticide, cyflumetofen (2-methoxyethyl α-cyano-α-[4-(1,1-dimethylethyl)phenyl]-β-oxo-2-(trifluoromethyl)benzenepropanoate) in or on tea at 40 parts per million (ppm). The high performance liquid chromatography-tandem mass spectrometry method is used to measure and evaluate the chemicals, cyflumetofen and 2-trifluoromethylbenzoic acid. *Contact:* RD.

2. *PP 4F8325*. (EPA–HQ–OPP–2017–0063). ICA Trinova, Inc., 1 Beavers Street, Suite B, Newnan, GA 30263, requests to establish a tolerance in 40 CFR part 180 for residues of the antimicrobial, sodium chlorite, in or on cantaloupes at 1.5 parts ppm. Liquid chromatography—mass spectroscopy (LC/MS) is used to measure and evaluate the chemical chlorate. Adequate enforcement methodology (LC/MS) is available to enforce the tolerance expression. The method may be requested from: Chief, Analytical Chemistry Branch, Environmental Science Center, 701 Mapes Rd., Ft. Meade, MD 20755–5350; telephone number: (410) 305–2905; email address: *residuemethods@epa.gov. Contact:* AD.

3. *PP 7F8558*. (EPA–HQ–OPP–2017–0233). Bayer CropScience, 2 T. W. Alexander Drive, Research Triangle Park, NC 27709 requests to establish a tolerance in 40 CFR part 180 for residues of the insecticide, tetraniliprole in or tuberous and corm vegetables, crop group 1C at 0.015 ppm; potato, wet peel at 0.02 ppm; leafy vegetables, crop group 4–16 at 20 ppm; brassica head and stem vegetables, crop group 5–16 at 1.5 ppm; fruiting vegetables, crop group 8–10 at 0.40 ppm; tomato paste at 1.5 ppm; citrus fruit, orange subgroup 10–10A at 0.50 ppm; citrus fruit, lemon/lime subgroup 10–10B at 0.80 ppm; citrus fruit, grapefruit subgroup 10–10C at 0.50 ppm; citrus oil at 4.0 ppm; pome fruit, crop group 11–10 at 0.40 ppm; stone fruit, crop group 12–12 at 1.0 ppm; plum, dried (prune) at 2.0 ppm; small fruit, vine climbing subgroup, except fuzzy kiwi, crop subgroup 13–07F at 1.5 ppm; tree nuts, crop group 14–12 at 0.03 ppm; almond hulls at 4.0 ppm; corn, field, grain at 0.015 ppm; corn, field, forage at 4.0 ppm; corn, field, stover at 15 ppm; corn, pop, grain at 0.015 ppm; corn, pop, stover at 15 ppm; corn, sweet, kernel plus cobs with husks removed at 0.01 ppm; corn, sweet, forage at 6.0 ppm; corn, sweet, stover at 20 ppm; cottonseed, crop group 20C at 0.40 ppm; cotton, gin byproducts at 30 ppm; soybean seed at 0.20 ppm; soybean hulls at 0.60 ppm; aspirated grain fractions at 45 ppm; soybean forage at 0.07 ppm; soybean hay at 0.20 ppm; alfalfa, forage and hay at 0.06 ppm; forage, fodder and straw of cereal grains, crop group 16, except field, pop and sweet corn at 0.10 ppm; foliage of legume vegetables, crop group 7, except soybeans at 0.03 ppm; milk at 0.06 ppm; fat of cattle, horses, sheep and goats at 0.30 ppm; muscle of cattle, horses, sheep and goats at 0.03 ppm; meat by-products of cattle, horses, sheep and goats at 0.30 ppm. The high performance liquid chromatography-electrospray ionization/tandem mass spectrometry (LC/MS/MS) is used to measure and evaluate the chemical. *Contact:* RD.

Authority: 21 U.S.C. 346a.

Dated: November 14, 2017.

Hammad A. Syed,

Acting Director, Information Technology and Resources Management Division, Office of Pesticide Programs.

[FR Doc. 2017–27103 Filed 12–14–17; 8:45 am]

BILLING CODE 6560–50–P

ENVIRONMENTAL PROTECTION AGENCY

[EPA–HQ–OPP–2015–0393; FRL–9970–54]

Interim Registration Review Decisions and Case Closures for Several Pesticides; Notice of Availability

AGENCY: Environmental Protectiou Agency (EPA).

ACTION: Notice.

SUMMARY: This notice announces the availability of EPA's interim registration review decision for the chemicals listed in the Table in Unit II of this Notice. It also announces the case closure for metiram (Case 0644 and Docket ID Number: EPA–HQ–OPP–2015–0290) because all of the U.S. registrations for this pesticide have been canceled. Registration review is EPA's periodic review of pesticide registrations to ensure that each pesticide continues to satisfy the statutory standard for registration; that is, the pesticide can perform its intended function without causing unreasonable adverse effects on human health or the environment. Through this program, EPA is ensuring that each pesticide's registration is based on current scientific and other knowledge, including its effects on human health and the environment.

SUPPLEMENTARY INFORMATION:

I. General Information

A. Does this action apply to me?

This action is directed to the public in general, and may be of interest to a wide range of stakeholders including environmental, human health, farm worker, and agricultural advocates; the chemical industry; pesticide users; and members of the public interested in the sale, distribution, or use of pesticides. Since others also may be interested, the Agency has not attempted to describe all the specific entities that may be affected by this action. If you have any questions regarding the applicability of this action to a particular entity, consult the pesticide specific contact person listed under **FOR FURTHER INFORMATION CONTACT**: *For pesticide specific information, contact:* The Chemical Review Manager for the pesticide of interest identified in the table in Unit II.

For general information on the registration review program, contact: Dana Friedman, Pesticide Re-Evaluation Division (7508P), Office of Pesticide Programs, Environmental Protection Agency, 1200 Pennsylvania Ave. NW, Washington, DC 20460–0001; telephone number: (703) 347–8827; email address: *friedman.dana@epa.gov.*

II. What action is the Agency taking?

Pursuant to 40 CFR 155.58(c), this notice announces the availability of EPA's interim registration review decision for the chemicals listed in the Table in Unit II.

Pursuant to 40 CFR 155.57, a registration review decision is the Agency's determination whether a pesticide meets, or does not meet, the standard for registration in Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA). EPA has considered the chemicals listed in the following Table in light of the FIFRA standard for registration. The interim registration review decisions are supported by rationales included in the docket established for each chemical.

In addition to the interim registration review decision document, the registration review docket for the chemicals listed in the Table also includes other relevant documents related to the registration review of these cases. The proposed interim registration review decision was posted to the docket and the public was invited to submit any comments or new information.

Boukedes, Alexandra

From: James Wagner <jmw@wagnerreg.com>
Sent: Tuesday, September 26, 2017 12:34 PM
To: Boukedes, Alexandra
Cc: Tom Hashman
Subject: RE: EPA's response to Envera's August 9, 2017, letter preliminarily responding to the EPA's July
Attachments: CONTRACT FOR STUDY AUTHORIZATION Envera - ENV503.pdf; IV Tox ENV503 DRAFT PROTOCOL Stillmeadow Lab.pdf

Importance: High

Hi Alex,

I am now providing Envera's final response to EPA's July 13, 2017, 75-day deficiency letter and the Agency's clarifying letter of September 8th.

To address and resolve the deficiency noted by the Agency, Envera has contracted with Stillmeadow Laboratory to conduct and report an acute injection/pathogenicity study, EPA guideline 885.3200 using *Bacillus amyloliquefaciens* strain ENV503. A copy of the draft study protocol with study number and a copy of the signed study contract are attached as supporting evidence that the study will be conducted. Envera commits to submit the study report upon its completion. The protocol proposes to initiate the study on or about November 13th with completion on or about December 15th. Based on these dates, we anticipate submission of the final report on or about January 15, 2018.

We trust that this action by Envera will enable the Agency to continue its review of the registration applications submitted for ENV503 without interruption. Please let me know if you require any further information regarding the scheduled study, including updates on study progress.

Thank you your help with Envera's applications.

Best regards,

Jim Wagner
Regulatory Consultant for Envera, LLC
Tel: (302) 635-7290
Mobile: (302) 530-5745

From: Boukedes, Alexandra [mailto:boukedes.alexandra@epa.gov]
Sent: Friday, September 08, 2017 5:45 PM
To: James Wagner <jmw@wagnerreg.com>
Subject: EPA's response to Envera's August 9, 2017, letter preliminarily responding to the EPA's July

Hi Jim,

Attached please find EPA's response to Envera's August 9, 2017, letter preliminarily responding to EPA's July 13, 2017, 75-day deficiency letter. Please let me know if you have any questions or concerns!

Best,
Alex

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-347-0305
boukedes.alexandra@epa.gov

CONTRACT FOR STUDY AUTHORIZATION

Date: _____ **S.D.** _____ **Code:** _____ **TM Rec.** _____

A. SPONSOR IDENTIFICATION AS IT SHOULD APPEAR IN PROTOCOL AND REPORT:

Sponsor Name (Company): Envera, LLC		
Address: 220 Garfield Ave. West Chester, PA 19380		
City: West Chester	*State:* PA	*Zip Code:* 19380
Country: USA	*Phone:* 484-593-0058	*Fax:*
Contact Name and Title: James Wagner	*E-Mail Address:* jmw@wagnerreg.com	

B. TEST MATERIAL NAME AS IT SHOULD APPEAR IN PROTOCOL AND REPORT:

Test Material Name: ENV503	*Technical Grade* ✓ *Or End Use Product* ☐ **MSDS should accompany the test material.** A Certificate of Analysis is required for all GLP studies****
Quantity: 100 grams	*Appearance:* tan powder
Expiration Date: 9/19/2018	*Storage Conditions:* cool less than 28C
Please indicate if the test material poses any health or safety concerns that may require special handling:	

C. STUDY TYPE /TEST SYSTEM

Will a pre- and post-toxicity analysis for stability be required? Yes ☐ No ✓	↓ STILLMEADOW, use only↓	
1.		
2.		
3.		
4.		
5.		
6		

D. FOR SUBMISSION TO ONE OR MORE OF THE FOLLOWING REGULATORY AGENCIES:

✓ EPA-OPPTS (FIFRA) - GLP ☐ OECD - GLP ☐ EPA -TSCA - GLP ☐ FDA – GLP

☐ FDA - CVM - GCP ☐ MAFF - GLP ☐ OTHER – SPECIFY _____

Countries intended for submission USA

**** A signed GLP statement **must** accompany the Certificate of Analysis in order to avoid compliance exceptions for characterization and stability.

E. DER (Data Evaluation Record) (Additional Charge) Yes ☐ No ✓

F. ADDITIONAL CHARGES

STILLMEADOW, Inc. will retain a reserve sample of each test material from regulatory studies for a minimum of five years. After testing, STILLMEADOW will dispose of unused test material. A minimum retention/disposal fee of $140.00 will be added to the final invoice to cover this expense. (Please include this fee in purchase orders.) By signing this authorization, sponsor (or sponsor's designee) agrees to pay for all work described herein and in the accompanying protocols. Additional charges may be made for draft and interim reports; extra copies, special formatting, express delivery, amendments, addenda to reports, and test material return. **Each protocol prepared is subject to a cancellation fee of at least $110.00.** Terms are Net 30.

G: Disposition of Unused Test Material: All unused test material will be properly disposed of by STILLMEADOW, Inc. unless arrangements are made at time of study authorization for Sponsor to pick-up unused test material at our facility in Sugar Land Texas.

Authorized by: James Wagner **Title:** Regulatory Consultant

Signature: James M Wagner **Date:** 9/19/2017

H. AGREEMENT BY SPONSOR TO PAY FOR THE SERVICES DESCRIBED ABOVE (If different from the authorizer):

Name (Printed): _____ **Title:** _____

Signature: _____ **Date:** _____

Rev. 15Jan16

I. SUPPLEMENTAL INFORMATION:

Mailing Address For Reports

Company Name Wagner Regulatory Associates		
Address: P.O. Box 640		
City: Hockessin	*State:* DE	*Zip Code:* 19707
Attention: James Wagner	*Electronic Copy Only:* ☐ **Yes** ☐ **No, send me a paper copy also**	

Billing Address

Company Name: Envera, LLC		*Attention:* Tom Hashman
Address: 220 Garfield Ave.		
City: West Chester	*State:* PA	*Zip Code:* 19380
Include e-mail address below if electronic copy of the invoice is acceptable. *Email:* thashman@envera.com	*Phone:* 484-593-0058	***Purchase Order No.***

A DEPOSIT OF THE ESTIMATED COST OF THE STUDY(S) MAY BE REQUIRED BEFORE STUDY(S) CAN BE INITIATED.

Send all documents and test samples to **STILLMEADOW, Inc.**
12852 Park One Drive
Sugar Land TX 77478
Ph. 281-240-8828 FAX 281-240-8448

J. COMMENTS

For STILLMEADOW Use Only:

DRAFT

PROTOCOL FOR STUDY 21337-17

Study Title: Intravenous Toxicity / Pathogenicity Study in Rats (OCSPP 885.3200)

Test Substance: ENV503

Test Facility: STILLMEADOW, Inc.
12852 Park One Drive
Sugar Land, TX 77478

Approved: _____ _____
Andrew Doig, MS
Study Director
STILLMEADOW, Inc.
Date

Approved: _____ _____
Mark Holbert
Vice President
STILLMEADOW, Inc.
Date

Reviewed: _____ _____
Kristina Rodrigue, RQAP- GLP
Director, Quality Assurance Unit
STILLMEADOW, Inc.
Date

Sponsor: Envera, LLC
220 Garfield Ave.
West Chester, PA 19380
484-593-0058
jmw@wagnerreg.com

Mail to: Attention: James Wagner
Wagner Regulatory Associates
P.O. Box 640
Hockessin, DE 19707

Approved: DRAFT DO NOT SIGN_____ _____
James M. Wagner
Regulatory Consultant
Date

PROTOCOL FOR STUDY 21337-17

A. GENERAL

1. Study Title: Intravenous Toxicity / Pathogenicity Study in Rats

2. Purpose: To evaluate the acute intravenous toxicity and infectivity of a microbial pest control agent (MPCA) at a single high dose exposure and an adequate post-exposure observation period.

3. Methods Guidelines: This study will be conducted according to OCSPP 885.3200.

4. Regulatory Compliance: This study will be conducted in compliance with Good Laboratory Practice Standards of EPA FIFRA, 40 CFR Part 160.

   In the event of a regulatory inspection, Regulatory Inspectors will be provided with all study documentation requested. The Sponsor will be notified of the inspection of their study.

   All procedures in this protocol are in compliance with Animal Welfare Act Regulations. All methods can be found in STILLMEADOW, Inc. Standard Operating Procedures (SOPs).

5. Quality Assurance: The Quality Assurance Unit (QAU) will review the protocol. The study information will be entered into the Master Schedule. In-progress inspection(s) will be performed to ensure the integrity of the study. Any deviations from SOPs, the Protocol or Good Laboratory Practice Standards will be immediately reported to the Study Director and Management. The report and raw data will be audited, and a statement prepared and signed that will specify the dates that the inspections were made and findings reported to Management and the Study Director.

6. MPCA Test Substance: ENV503. Test substance identification should include the name, batch number and purity. The Sponsor should also provide information regarding safety, stability, storage conditions and disposal. The Sponsor assumes responsibility for purity, stability, identity, synthesis methods and location of documentation.

7. Control Substance: Inactivated ENV503. Inactivated by STILLMEADOW, Inc. by autoclaving the test substance.

8. Proposed Schedule: Proposed Experimental Start Date: 13 Nov 17
   Proposed Experimental End Date: 15 Dec 17

   The in-life portion of the study will be at least 21 days.

A. GENERAL (cont.)

9. Study Director: Andrew Doig, MS

10. Experimental Summary: The MPCA test substance or inactivated MPCA test substance will be injected into the tail vein of one of two groups of rats at a high dose. The animals will be observed frequently on day of dosing for mortality and signs of pharmacologic and/or toxicologic effects and once daily thereafter for the duration of the study. A control group (untreated) will be conducted concurrently. Tissue and blood samples collected during the study will be cultured to provide quantitative measurements of the test microbe.

11. Protocol Amendments: Any alteration in the Protocol will be justified, approved by the Study Director and recorded in writing.

12. Sponsor Audits: The Sponsor may send an authorized representative to inspect the test system and/or data on the STILLMEADOW, Inc. premises during normal working hours.

B. EXPERIMENTAL DESIGN

1. Animals

a. Species/Strain/Source: Albino rat; Sprague-Dawley; Texas Animal Specialties., Humble TX (or other suitable supplier)

b. Justification of Species: The rat is conventionally used to provide an index of toxicity on which human hazard can be judged, and is the species preferred by the regulatory agencies.

c. Quantity and Sex: 28 males and 28 females (nulliparous and non-pregnant) and 3 validation animals

d. Age/Weight: Young adult (7-12 weeks)
Males: 225-375 grams; Females: 150 - 250 grams
Weight variation should not exceed ±20% of the mean for each sex.

e. Identification: Ear punch and cage cards

f. Acclimation and Health Status: Animals will be acclimated for at least 5 days prior to testing. Normal weight gain, appearance and behavior will be factors used to select healthy animals for testing. Only naive animals will be selected.

B. EXPERIMENTAL DESIGN (cont.)

2. Animal Husbandry

a. Cages:	Polycarbonate boxes with bedding
b. Number per Cage:	Animals will be housed individually during the study.
c. Enrichment:	Provided to each animal during study; for example plastic PVC pipe pieces.
d. Food:	PMI Feeds, Inc.™ Formulab #5008, available *ad libitum*. Analyzed by manufacturer.
e. Water:	Tap water; available *ad libitum* (automatic system). Municipal water supply analyzed by Texas Commission on Environmental Quality (TCEQ) Water Utilities Division.
f. Contaminants:	There are no known contaminants in the feed or water available to laboratory animals that would be expected to interfere with this study.
g. Environment:	Room temperature of 22°C ±3°C Relative humidity of 30 - 70% 12-hour light/dark cycle (regulated automatically) Room ventilation of ≥10 air changes per hour

3. Growth Conditions

a. Media:	Media to be used
b. Incubator Temperature:	00±2°C

4. Test Substance Administration

a. Reason for Route of Administration:	Historically, the intravenous route has been a route of choice for evaluation of the toxicity potential of a test substance and is a potential route of human exposure.
b. Validation of Test Organism Recovery:	Prior to or concurrent with the enumeration of Day 0 test samples, the test organism will be used to spike the tissues of three additional untreated animals to assure adequate recovery of the test organism should it occur in the lungs, liver, cecum contents, and blood. The tissue specimens will be homogenized and the test organism serially diluted for enumeration by plate count; the mean will be compared to the predicted count and percent recovery will be determined. To determine the effect of the homogenization step on viability of the test organism, the organism stock suspension will be subsampled and subjected to homogenization by the same method used for the specimens. The suspended test organism stock, the homogenized stock suspension, the homogenized specimens without the test organism, and the homogenized spiked specimens will be serially diluted and plated on the appropriate agar. Percent recovery of the test organism will be calculated. If this information has been obtained in a recent study at STILLMEADOW, Inc. with the same test organism for the same Sponsor, this determination need not be repeated.

B. EXPERIMENTAL DESIGN (cont.)

4. Test Substance Administration (cont.)

c. Test Substance Preparation: The test substance will be prepared by diluting the test substance supplied by the sponsor, using sterile phosphate buffered saline to an appropriate consistency and concentration for dosing.

d. Test Substance Analysis: Prior to administration of the test and control substances, samples will be taken for analysis to quantify the number of viable test microbes in the test substance (MPCA) mixture and to confirm the absence of viable test microbes in the control substance (inactivated MPCA). One unit of representative MPCA is a single Colony Forming Unit (CFU). CFUs will be quantified using the appropriate growth media and the plate count method.

e. Preparation of Control Substance: A portion of the MPCA test substance dosing solution will be rendered nonviable by autoclaving, performed by STILLMEADOW, Inc. personnel, to yield the inactivated MPCA.

f. Dosing: After sterilizing the injection site with alcohol, the test substance or inactivated test substance will be administered intravenously into the tail vein. Group I will not be dosed.

g. Satellite Group: Three males and three females in Group IV will be dosed on Day 0 with the active test substance and designated as a satellite group. If the animals sacrificed on Day 21 do not show evidence of clearance or a pattern of clearance, then this satellite group will be maintained until a sacrifice date to be determined by the Study Director (in consultation with the Sponsor). If the tissues from Group III animals sacrificed on Day 21 show evidence of clearance or a pattern of clearance at the Day 21 plate counts, then the satellite group (Group IV) will be sacrificed after the plate counts for Group III are complete and no necropsy, final body weight or quantification will be conducted.

B. EXPERIMENTAL DESIGN (cont.)

4. Test Substance Administration (cont.)

h. Experimental Design: There will be four groups of animals that will run concurrently. Groups I will be untreated controls. Group II will receive the inactivated MPCA. Interim sacrifices are outlined in the following schedule. Group III and Group IV animals will receive the test substance.

Group	Substance	Dose CFU/rat	M/F on Test	M/F on Day 0*	M/F on Day 3	M/F at Week 1	M/F at Week 2	M/F at Week 3	M/F Satellite
I	Untreated	-	5/5					5/5	
II	Inactive	@	5/5					5/5	
III	MPCA	$\geq 10^7$	15/15	3/3*	3/3	3/3	3/3	3/3	
IV	MPCA - Sat	$\geq 10^7$	3/3						3/3

@ - Dose volume equivalent to that received by Group III
MPCA - Microbial Pest Control Agent
CFU - Colony forming unit
M/F - Males/Females
* - Following dosing
Sat - Satellite
Satellite - If the Day 21 tissues from Group III do not show evidence of clearance or a pattern of clearance, then the satellite group will be maintained and sacrificed at a later time point to be determined by the study director (in consultation with the Sponsor). Otherwise, the satellite group will be sacrificed after the Group III Day 21 plate counts are complete.
Additionally, 3 untreated animals will be used for validation of test organism recovery.

5. Observations

a. Clinical Signs: Observations for mortality and signs of pharmacologic and/or toxicologic effects will be made three times on Day 0 following dosing and once daily thereafter for the duration of the study. The nature, onset, severity and duration of all gross or visible pharmacologic or toxicologic signs will be recorded.

Cage side observations shall include, but will not be limited to: skin and fur; eyes and mucus membranes; respiratory, circulatory, autonomic and central nervous systems; somatomotor activity and behavior patterns. Particular attention shall be given to tremors, convulsions, salivation, diarrhea, lethargy, sleep and coma.

b. Body Weights: Body weights and time taken will be recorded on Day 0, prior to dosing, and weekly thereafter (Days 7, 14 and 21) or at the time of sacrifice or discovery after death. If the study is extended, body weights will continue to be taken weekly.

c. Necropsy: A gross necropsy will be conducted on each animal sacrificed at the interim times, with the exception of Day 0 animals from whom only blood will be drawn, and at termination of the study or at the time of discovery after death. The gross necropsy shall include the following: gross observations of external surfaces; all orifices; thoracic, abdominal and pelvic cavities.

B. EXPERIMENTAL DESIGN (cont.)

5. Observations (cont.)

d. Interim and Final Sacrifice Analyses: Group III animals will have the following tissue and fluid samples taken at the time of scheduled sacrifice (beginning at Day 3).

1. One mL of blood.

2. Brain, lungs, liver, spleen, kidneys, lymph nodes and cecum content sample will be removed and weighed. Cecum contents will only be weighed if intended for plating. A 1 g sample of any abnormal tissue may be saved in 10% neutral buffered formalin for possible future histopathologic examination at the request of the sponsor. Saved samples will be sent to Colorado Histo-Prep, Fort Collins, CO (or other suitable laboratory) for histopathologic evaluation at request of the sponsor. Tissues will be discarded if histopathology is not performed.

All tissue and fluid samples removed for quantification will be cultured according to STILLMEADOW, Inc. SOPs, using suitable media to provide qualitative and quantitative measurements of the test microbe. Samples will be plated in triplicate and placed in an incubator until colony growth is sufficient for accurate enumeration.

e. Clearance of MPCA from Blood: Three males and three females from the Group III will be sacrificed on Day 0 (as soon after dosing as possible), and 1 mL of blood will be analyzed for the presence of MPCA. Blood from animals sacrificed at subsequent interim and final sacrifices will be examined for the presence of MPCA to estimate clearance of the MPCA after dosing.

6. Evaluation of Results: An evaluation will be made of the relationship, if any, between exposure to the test substance and the incidence and severity of all abnormalities including: behavior, body weight changes, mortality, gross lesions and toxicity, infectivity and pathogenicity. The data will be evaluated for the rate of test organism clearance. When possible, the effects of treatment will be determined by appropriate statistical methods comparing treatment groups. When organ weights are statistically compared, organ weights relative to body weights will be used.

B. EXPERIMENTAL DESIGN (cont.)

7. Test Substance Accountability:

A comprehensive inventory of test substance received and used will be kept. The test substance container(s) will be weighed when received at this facility, and a record of all test substance use will be maintained. Test substance and test substance dosing solutions will be stored in the original containers, or in the equivalent thereof, or in glass containers with Teflon-lined caps.

8. Disposal of Unused Test Substance:

Unused test substance will be disposed of at the Sponsor's expense after the termination of the study. A reserve sample of dry test substances will be retained by STILLMEADOW, Inc. for at least five years.

9. Safety Precautions:

General safety precautions required by laboratory SOPs will be followed. The Sponsor will supply basic toxicity data on the test substance to be used. However, since the toxicity of test substances is often not well characterized, this laboratory will be conservative in setting safety procedures. The Sponsor or Sponsor's Representative shall be notified of any exposures requiring a physician's examination or care.

C. DATA MANAGEMENT

1. Records:

The following records will be maintained during the study and archived at STILLMEADOW, Inc. upon study termination:

a. Protocol and Protocol Amendments (if any)
b. Final report and amendments (if any)
c. Study correspondence
d. Animal receipt/acclimation data
e. Test substance receipt, identification as supplied by Sponsor, preparation, administration and disposition
f. Test animal information: number, sex, source, strain
g. Body weight data
h. Daily observation data for signs of pharmacologic and/or toxicologic effects
i. Mortality data, gross necropsy findings and histopathology findings, if requested
j. Microbial data from MPCA and inactivated MPCA samples, and tissue, organ and blood samples
k. Other pertinent data

C. DATA MANAGEMENT (cont.)

2. Data Storage: All raw data, and originals of both the protocol and final report will be archived at STILLMEADOW, Inc. for at least 5 years.

3. Data Reporting: The final report will include all data as described in the Good Laboratory Practice Standards, including:

a. Statement from the Quality Assurance Unit
b. Signature of the Study Director
c. A GLP Compliance Statement signed by the Study Director
d. Names of scientific personnel involved in the study
e. Dates of study initiation and termination
f. Identification, label information, description, preparation and storage of the test substance
g. All pertinent animal data, animal husbandry, dosing information and observation methods
h. Description of test procedures
i. Individual body weights and weight changes and time taken
j. Individual mortality data and gross necropsy findings
k. Observations on the nature, onset, severity and duration of all gross or visible pharmacologic and/or toxicologic signs
l. Microbial data from MPCA and inactivated MPCA samples; tissue, organ and blood samples
m. Infectivity/persistence findings and estimate of rate of MPCA clearance
n. Description of all enumeration methods used for MPCA detection and quantification
o. Verification that each enumeration method is sufficiently sensitive to serve as a useful quantitative assay, for the MPCA in tissues, organ and body fluids, if available.
p. A copy of this Protocol.
q. Any protocol deviations and the impact, if any, on the study

4. Report Submission: A report will be submitted after termination of the in-life portion of the study (subject to completion of histopathology, if requested). In the event that a draft report is issued, there will be a 90-day Sponsor approval period. The report will be finalized upon Sponsor approval or at the end of the 90-day period.

Docket Verification and Certification Form

For Internal OCSPP Use Only
U.S. Environmental Protection Agency
Office of Chemical Safety and Pollution Prevention
1200 Pennsylvania Avenue, N.W., Washington, D.C. 20460

Title of Action: Receipt of Several Pesticide Petitions Filed for Residues of Pesticide Chemicals in or on Various Commodities

Docket Type: (●) Rulemaking ( ) General ( ) Docket does not involve an FR Notice

Docket ID #: EPA-HQ-OPP-2017-0460 RIN #: FRL #:

Docket Title: Exemption from the Requirement of a Tolerance (Bacillus amyloliquefaciens ENV503 – FFDCA)

☐ Are Multiple Dockets Listed in this Federal Register? If Checked, List All Docket Numbers in this Federal Register:

Contact Name: Alexandra Boukedes Contact Phone: 703-347-0305

Program Lead's Verification: I have reviewed the docket and verified the following: *(check all that apply)*

☐ Documents containing copyrighted, CBI or otherwise protected information have been identified to allow for 'special' processing by the docket.

☒ All documents have been added to the Docket(s) in FDMS.

1 Enter number of supporting documents added to the Docket(s) in FDMS for this action.

☐ No supporting materials for this action.

Comments:

Email this form to the OCSPP Docket Manager for the Docket Manager's Verification signature. Email to OCSPP Docket Manager

Signature: ALEXANDRA BOUKEDES Digitally signed by ALEXANDRA BOUKEDES Date: 2017.08.24 07:54:21 -04'00' Date: 08/24/2017

Docket Manager's Verification: I hereby confirm the following: *(check all that apply)*

☑ The Docket ID number(s) identified above matches our records.

☑ The correct number of supporting documents for this action (as indicated above) are present in the FDMS Docket(s).

Comments:

Signature: Arletha Bates Date: 9/26/17

This section should be completed only after the docket's verification has been received and any noted deficiencies have been resolved. Do not provide certification until the cited materials are assembled for the final signature package.

Program Lead's Certification: I hereby certify that: *(check all that apply)*

☑ I have completed the verification above.

☑ I have submitted to FDMS all of the documents that I identified for inclusion in the Docket(s).

☑ The Docket is complete and ready for public release.

Comments:

Signature: Alyndra Boukedes Date: 9/26/17

Rev 8.9.13

Boukedes, Alexandra

From: Boukedes, Alexandra
Sent: Wednesday, September 13, 2017 11:30 AM
To: Zuber, Mohammed
Subject: Contractor DERs for BAM ENV 503
Attachments: DER for MRID 50159801 (BAM ENV 503 MUP).docx; DER for MRID 50159802 (BAM ENV 503 MUP).docx; DER- PCHEM BAM ENV 503 EP.DOCX; DER- PCHEM BAM ENV 503 MUP.DOCX; BPPD Contractor Request Form_B. amyloliquefaciens ENV503_87645-G 87645-....pdf

Hi Mohammed,

Attached you will find the contractor DERs for BAM ENV 503. Please review the DERs and complete the last page of the BPPD contractor request form. When you have completed the BPPD contractor request form send it back to me. If there are any problems with the DERs let me know so we can get them fixed.

Thanks,
Alex

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-347-0305
boukedes.alexandra@epa.gov

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

September 8, 2017

BY EMAIL

James M. Wagner
Authorized Agent to Envera, LLC (Envera)
Wagner Regulatory Associates, Inc.
P.O. Box 640
Hockessin, DE 19707

Re: EPA's response to Envera's August 9, 2017, letter preliminarily responding to the EPA's July 13, 2017, 75-day deficiency letter (EPA File Symbols: 87645-G and 87645-U; Pesticide Petition No. 7F8546) (OPP Decision Nos. 526002, 526004, and 526003)

Dear Mr. Wagner:

The U.S. Environmental Protection Agency (EPA) has reviewed your preliminary response to its July 13, 2017, 75-day deficiency letter and has concluded that you still need to submit data obtained from a toxicity/pathogenicity study (including clearance data) for acute pulmonary toxicity/pathogenicity (Guideline 885.3150) or acute injection toxicity/pathogenicity (Guideline 885.3200) using *Bacillus amyloliquefaciens* strain ENV503 as the test substance. The EPA will also accept data (including clearance data) obtained, as a third option, from an acute oral toxicity/pathogenicity study (Guideline 885.3050) using *Bacillus amyloliquefaciens* strain ENV503 as the test substance.

As explained in the EPA's 75-day deficiency letter, when an applicant isolates a microorganism from another company's product and aims to rely on the other company's generic data (e.g., toxicological data), the EPA generally asks that (1) detailed product identity information and (2) a bridging study (i.e., a toxicity/pathogenicity study done with the applicant's microorganism) be provided.

Furthermore, pursuant to 40 CFR § 158.2100(c)(2), "Each new isolate of a microbial pesticide is a new active ingredient and must be registered independently of any similarly designated and already registered microbial pesticide active ingredient. Each new isolate for which registration is sought must have a unique identifier following the taxonomic name of the microorganism, and the registration application must be supported by data required in this subpart. **This does not preclude the possibility of using data from another isolate, provided sufficient similarity is established, to support registration**." (emphasis added)

While Envera has provided genome sequencing data to confirm that *Bacillus amyloliquefaciens* strain ENV503 and the active ingredient from the source product are similar, this is only half of the data the EPA needs to determine whether *Bacillus amyloliquefaciens* strain ENV503 is sufficiently similar to the active ingredient found in the source product; the other part of the data needed to determine if *Bacillus amyloliquefaciens* strain ENV503 is sufficiently similar to the active ingredient in the source product is a toxicity/pathogenicity study.

Again, as stated in the 75-day deficiency letter, the EPA recognizes that, with the previous *Bacillus amyloliquefaciens* strain ENV503 application that was rejected in 2015 (EPA File Symbol: 87645-E), it did not inform you appropriately of the need for a bridging study. We have now done so and will continue with the review of the current applications, if you submit data obtained from a toxicity/pathogenicity study (including clearance data) for acute pulmonary toxicity/pathogenicity (Guideline 885.3150), acute injection toxicity/pathogenicity (Guideline 885.3200), or acute oral toxicity/pathogenicity (Guideline 885.3050) using *Bacillus amyloliquefaciens* strain ENV503 as the test substance. While you have the option of conducting any of the toxicity/pathogenicity studies, the acute injection toxicity/pathogenicity study is preferable. An acceptable toxicity/pathogenicity study (as described above), in conjunction with your product identity information, will provide confidence to the EPA that the data generated using *Bacillus subtilis* strain GB03 as the test substance and to which you cite are adequate to support your applications.

Many small businesses, like yours, operate within the highly regulated biopesticide market. The EPA recognizes the important advantage of the overall reduced risk aspects of biopesticides and has tried to create a market that allows entry to businesses of all financial sizes. The EPA achieves this goal by requiring data sets for biopesticides that are significantly smaller than the data sets used to regulate antimicrobial or conventional pesticides. In addition, the EPA also allows citation to peer-reviewed literature to satisfy many biopesticide data requirements. Out of the limited data set provided to support registration of biopesticides, the EPA is asking you to submit one study to bridge your new active ingredient *Bacillus amyloliquefaciens* strain ENV503 to all the *Bacillus subtilis* strain GB03 data to which you are citing. As stated above, you have been informed of the requirement for a bridging study, and the EPA will continue with its review of the current applications if you submit such study.

This is the EPA's detailed technical position on why you must provide data obtained from a toxicity/pathogenicity study (including clearance data) using *Bacillus amyloliquefaciens* strain ENV503 as the test substance. Please note that the EPA does not consider your preliminary response to be the formal response to the July 13, 2017, 75-day deficiency letter and that you must provide this, as previously described in the 75-day deficiency letter, by September 26, 2017.

If you have questions concerning this letter, please contact Alex Boukedes by telephone at (703) 347-0305 or via email at boukedes.alexandra@epa.gov.

Sincerely,

Jeannine Kausch, Product Manager 92
Microbial Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)
Office of Pesticide Programs

WRA
Wagner Regulatory Associates, Inc.
P.O. Box 640
7217 Lancaster Pike, Suite A
Hockessin, Delaware 19707

Federal Express and Email

August 9, 2017

Jeannine Kausch, Product Manager 92
Microbial Pesticides Branch, BPPD (7511P)
Office of Pesticide Programs
US Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Re: Your letter of July 13, 2017 for ENV503 Biofungicide (87645-G, -U, and Petition 7F8546)

Dear Ms. Kausch,

On behalf of Envera, LLC, I am submitting this preliminary response to your 75-day deficiency letter received at this office on July 26, 2017, copy attached.

As a small business in a highly regulated field, Envera is dependent on reliable EPA guidance to successfully develop and market its microbial pesticides. We are therefore greatly disappointed that you now reject the guidance that BPPD provided to Envera at the 2015 meeting regarding data required to support the registration of this product. The Agency advice provided at the 2015 meeting was clear and unequivocal that the identification techniques used for ENV503 were sufficient to confirm that ENV503 and the source product are the same species and strain of *Bacillus amyloliquefaciens*. And further, that having proved the identification to the strain level, that bridging to the acute toxicity of the source product would be acceptable to support the registration of ENV503. This new request for additional toxicity data for ENV503, in our view, is inconsistent with the Agency's published strategic vision for reducing redundant and unnecessary animal toxicity testing.

Before providing a final response to the 75 day letter, we respectfully request a response to the following question submitted in our May 31, 2017 response to the 10 day deficiency letter, copy attached. The question is, if BPPD has changed its technical position provided at the 2015 meeting we request that the detailed technical basis for the change be provided so that we can review it. We would appreciate receiving your answer to this question so that we may prepare our final response to the 75 day letter.

Thank you for your consideration in this matter.

Sincerely,

James M. Wagner

James M. Wagner
Agent for Envera, LLC
Tel: (302) 635-7290
Email: jmw@wagnerreg.com

Enclosures

cc: Tom Hashman, Michael Matheny, Envera

RECEIVED
JUL 26 2017
By CN

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

July 13, 2017

~~**CONTAINS CONFIDENTIAL BUSINESS INFORMATION**~~

BY CERTIFIED MAIL
RETURN RECEIPT REQUESTED

James M. Wagner
Authorized Agent to Envera, LLC
Wagner Regulatory Associates, Inc.
P.O. Box 640
Hockessin, DE 19707

Subject: 75-day Deficiency: Acute Toxicity/Pathogenicity Study

Application for Registration Dated January 23, 2017
EPA Receipt Date: January 24, 2017
Product Name: ENV503 Biofungicide MUP
EPA File Symbol: 87645-G
OPP Decision Number: 526002

Application for Registration Dated January 23, 2017
EPA Receipt Date: January 24, 2017
Product Name: ENV503 Biofungicide Wettable Powder
EPA File Symbol: 87645-U
OPP Decision Number: 526004

Pesticide Petition for a Tolerance Exemption Dated January 23, 2017
EPA Receipt Date: January 24, 2017
Pesticide Petition Number: 7F8546
OPP Decision Number: 526005

Dear Mr. Wagner:

The U.S. Environmental Protection Agency (EPA or Agency) has received and begun its in-depth review of the subject applications and has determined that they are incomplete and that further information is needed. This letter is a written notification of that deficiency and identifies your options under 40 CFR § 152.105.

At this time, the EPA has identified the following deficiency in its review of the subject applications:

The EPA reviewed the minutes of the September 29, 2015, meeting that you attached as an appendix to MRID No. 501598-04, as well as its own records, and respectfully disagrees with your contention from your response to the May 10, 2017, 10-day deficiency letter that further identification and toxicity data are not needed to support these applications.

In situations, like this one, where an applicant isolates a microorganism from another company's product and aims to rely on the other company's generic data (e.g., toxicological data), the EPA generally asks that detailed product identity information and a bridging study (i.e., a toxicity/pathogenicity study done with the applicant's microorganism) be provided. The EPA recognizes that, with the previous *Bacillus amyloliquefaciens* strain ENV503 application that was rejected in 2015 (EPA File Symbol: 87645-E), it did not inform you appropriately of the need for a bridging study. We have now done so and will continue with the review of the current applications, if you submit data obtained from a toxicity/pathogenicity study (including clearance data) for acute pulmonary toxicity/pathogenicity (Guideline 885.3150) or acute injection toxicity/pathogenicity (Guideline 885.3200) using *Bacillus amyloliquefaciens* strain ENV503 as the test substance. While you have the option of conducting either toxicity/pathogenicity study, the acute injection toxicity/pathogenicity study is preferable. An acceptable toxicity/pathogenicity study (as described above), in conjunction with your product identity information, will provide confidence to the EPA that the data generated using *Bacillus subtilis* strain GB03 as the test substance and to which you cite are adequate to support your applications.

Further review of your applications and your response to the deficiency may identify additional deficiencies and you will be so informed.

In accordance with 40 CFR § 152.105, you are allowed 75 days from the date of this letter to provide a response concerning the deficiency listed in this letter. Please ensure that you consider each of the options below in determining how and when you respond to this letter. You have the following three options:

1. **Resolve the Issue.** You may resolve the issue by submitting a correction or an addition to complete the applications by September 26, 2017, or you may submit an explanation of why it will take longer than 75 days to address the deficiency. For the latter option, your explanation must include a written commitment and schedule for submitting the remaining information and/or data. When submitting information and/or data in response to this letter, a copy of this letter should accompany the submission to facilitate processing.

2. **Withdraw the Applications.** You may withdraw your applications. If fees were paid, the EPA will provide any applicable refund as soon as practicable.[1] A withdrawal concludes the EPA's review of your applications. Any subsequent submission of the same applications must then be submitted as new applications with new deadlines for the EPA to make determinations on your applications and, as applicable, subject to new registration service fees.

[1] See http://www2.epa.gov/pria-fees/overview-pria-fee-reduction-and-refund-formula for more information on refunds.

3. **Not Respond Properly.** If you do not respond to this letter by September 26, 2017, or if you respond with a date on which you expect to complete the applications but fail to meet that scheduled date, the EPA will administratively withdraw your applications. If fees were paid, the EPA will provide any applicable refund as soon as practicable.[2] A withdrawal concludes the EPA's review of your applications. Any subsequent submission of the same applications must then be submitted as new applications with new deadlines for the EPA to make determinations on your applications and, as applicable, subject to new registration service fees.

If you have any questions concerning this letter, please contact Alex Boukedes by telephone at (703) 347-0305 or via email at boukedes.alexandra@epa.gov.

Sincerely,

Jeannine Kausch, Product Manager 92
Microbial Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)
Office of Pesticide Programs

[2] See footnote #1.

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Alexandra Boutedes
U.S. Environmental Protection Agency
Office of Pesticide Programs 7511P
1200 Pennsylvania Ave, NW
Washington DC
20004

AUG 08 2017

SENDER: *COMPLETE THIS SECTION*

- Complete items 1, 2, and 3. Also complete item 4 if Restricted Delivery is desired.
- Print your name and address on the reverse so that we can return the card to you.
- Attach this card to the back of the mailpiece, or on the front if space permits.

1. Article Addressed to:

James M Wagner
Wagner Regulatory Associates, Inc
P.O. Box 640
Hockessin, DE
19707

COMPLETE THIS SECTION ON DELIVERY

A. Signature
X Carrie Nolan ☐ Agent ☐ Addressee

B. Received by (Printed Name) Carrie Nolan
C. Date of Delivery

D. Is delivery address different from item 1? ☐ Yes
If YES, enter delivery address below: ☐ No

3. Service Type
☒ Certified Mail ☐ Express Mail
☐ Registered ☒ Return Receipt for Merchandise
☐ Insured Mail ☐ C.O.D.

4. Restricted Delivery? (Extra Fee) ☐ Yes

2. Article Number (Transfer from service label) 7008 3230 0000 9475 1506

PS Form 3811, February 2004 Domestic Return Receipt 102595-02-M-1540

Federal Express and Email

August 9, 2017

WRA

Wagner Regulatory Associates, Inc.
P.O. Box 640
7217 Lancaster Pike, Suite A
Hockessin, Delaware 19707

Jeannine Kausch, Product Manager 92
Microbial Pesticides Branch, BPPD (7511P)
Office of Pesticide Programs
US Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Re: Your letter of July 13, 2017 for ENV503 Biofungicide (87645-G, -U, and Petition 7F8546)

Dear Ms. Kausch,

On behalf of Envera, LLC, I am submitting this preliminary response to your 75-day deficiency letter received at this office on July 26, 2017, copy attached.

As a small business in a highly regulated field, Envera is dependent on reliable EPA guidance to successfully develop and market its microbial pesticides. We are therefore greatly disappointed that you now reject the guidance that BPPD provided to Envera at the 2015 meeting regarding data required to support the registration of this product. The Agency advice provided at the 2015 meeting was clear and unequivocal that the identification techniques used for ENV503 were sufficient to confirm that ENV503 and the source product are the same species and strain of *Bacillus amyloliquefaciens*. And further, that having proved the identification to the strain level, that bridging to the acute toxicity of the source product would be acceptable to support the registration of ENV503. This new request for additional toxicity data for ENV503, in our view, is inconsistent with the Agency's published strategic vision for reducing redundant and unnecessary animal toxicity testing.

Before providing a final response to the 75 day letter, we respectfully request a response to the following question submitted in our May 31, 2017 response to the 10 day deficiency letter, copy attached. The question is, if BPPD has changed its technical position provided at the 2015 meeting we request that the detailed technical basis for the change be provided so that we can review it. We would appreciate receiving your answer to this question so that we may prepare our final response to the 75 day letter.

Thank you for your consideration in this matter.

Sincerely,

James M Wagner

James M. Wagner
Agent for Envera, LLC
Tel: (302) 635-7290
Email: jmw@wagnerreg.com

Enclosures

cc: Tom Hashman, Michael Matheny, Envera

RECEIVED
JUL 26 2017
By CS

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

July 13, 2017

~~**CONTAINS CONFIDENTIAL BUSINESS INFORMATION**~~

BY CERTIFIED MAIL
RETURN RECEIPT REQUESTED

James M. Wagner
Authorized Agent to Envera, LLC
Wagner Regulatory Associates, Inc.
P.O. Box 640
Hockessin, DE 19707

Subject: 75-day Deficiency: Acute Toxicity/Pathogenicity Study

Application for Registration Dated January 23, 2017
EPA Receipt Date: January 24, 2017
Product Name: ENV503 Biofungicide MUP
EPA File Symbol: 87645-G
OPP Decision Number: 526002

Application for Registration Dated January 23, 2017
EPA Receipt Date: January 24, 2017
Product Name: ENV503 Biofungicide Wettable Powder
EPA File Symbol: 87645-U
OPP Decision Number: 526004

Pesticide Petition for a Tolerance Exemption Dated January 23, 2017
EPA Receipt Date: January 24, 2017
Pesticide Petition Number: 7F8546
OPP Decision Number: 526005

Dear Mr. Wagner:

The U.S. Environmental Protection Agency (EPA or Agency) has received and begun its in-depth review of the subject applications and has determined that they are incomplete and that further information is needed. This letter is a written notification of that deficiency and identifies your options under 40 CFR § 152.105.

At this time, the EPA has identified the following deficiency in its review of the subject applications:

The EPA reviewed the minutes of the September 29, 2015, meeting that you attached as an appendix to MRID No. 501598-04, as well as its own records, and respectfully disagrees with your contention from your response to the May 10, 2017, 10-day deficiency letter that further identification and toxicity data are not needed to support these applications.

In situations, like this one, where an applicant isolates a microorganism from another company's product and aims to rely on the other company's generic data (e.g., toxicological data), the EPA generally asks that detailed product identity information and a bridging study (i.e., a toxicity/pathogenicity study done with the applicant's microorganism) be provided. The EPA recognizes that, with the previous *Bacillus amyloliquefaciens* strain ENV503 application that was rejected in 2015 (EPA File Symbol: 87645-E), it did not inform you appropriately of the need for a bridging study. We have now done so and will continue with the review of the current applications, if you submit data obtained from a toxicity/pathogenicity study (including clearance data) for acute pulmonary toxicity/pathogenicity (Guideline 885.3150) or acute injection toxicity/pathogenicity (Guideline 885.3200) using *Bacillus amyloliquefaciens* strain ENV503 as the test substance. While you have the option of conducting either toxicity/pathogenicity study, the acute injection toxicity/pathogenicity study is preferable. An acceptable toxicity/pathogenicity study (as described above), in conjunction with your product identity information, will provide confidence to the EPA that the data generated using *Bacillus subtilis* strain GB03 as the test substance and to which you cite are adequate to support your applications.

Further review of your applications and your response to the deficiency may identify additional deficiencies and you will be so informed.

In accordance with 40 CFR § 152.105, you are allowed 75 days from the date of this letter to provide a response concerning the deficiency listed in this letter. Please ensure that you consider each of the options below in determining how and when you respond to this letter. You have the following three options:

1. **Resolve the Issue.** You may resolve the issue by submitting a correction or an addition to complete the applications by September 26, 2017, or you may submit an explanation of why it will take longer than 75 days to address the deficiency. For the latter option, your explanation must include a written commitment and schedule for submitting the remaining information and/or data. When submitting information and/or data in response to this letter, a copy of this letter should accompany the submission to facilitate processing.

2. **Withdraw the Applications.** You may withdraw your applications. If fees were paid, the EPA will provide any applicable refund as soon as practicable.[1] A withdrawal concludes the EPA's review of your applications. Any subsequent submission of the same applications must then be submitted as new applications with new deadlines for the EPA to make determinations on your applications and, as applicable, subject to new registration service fees.

[1] See http://www2.epa.gov/pria-fees/overview-pria-fee-reduction-and-refund-formula for more information on refunds.

3. **Not Respond Properly.** If you do not respond to this letter by September 26, 2017, or if you respond with a date on which you expect to complete the applications but fail to meet that scheduled date, the EPA will administratively withdraw your applications. If fees were paid, the EPA will provide any applicable refund as soon as practicable.[2] A withdrawal concludes the EPA's review of your applications. Any subsequent submission of the same applications must then be submitted as new applications with new deadlines for the EPA to make determinations on your applications and, as applicable, subject to new registration service fees.

If you have any questions concerning this letter, please contact Alex Boukedes by telephone at (703) 347-0305 or via email at boukedes.alexandra@epa.gov.

Sincerely,

Jeannine Kausch, Product Manager 92
Microbial Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)
Office of Pesticide Programs

[2] See footnote #1.

Submitted Electronically

May 31, 2017

WRA
Wagner Regulatory Associates, Inc.
P.O. Box 640
7217 Lancaster Pike, Suite A
Hockessin, Delaware 19707

Document Processing Desk (REGFEE)
Attn: Jeannine Kausch, Microbial Pesticide Branch
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Re: ENV503 Biofungicide MUP (87645-G) and ENV503 Biofungicide Wettable Powder (87645-U)
Response to EPA 10-day deficiency letter of 10 May 2017

Dear Ms. Kausch,

On behalf of Envera LLC, I am responding to your deficiency letter of May 10, 2017, regarding the referenced products.

ENV 503 Biofungicide MUP - 87645-G

Response to each deficiency is provided below.

- Label deficiency – sub-label B for seed treatments has been deleted from the MUP label and moved to the label for 87645-U. Revised labels are attached.
- Data matrix deficiencies 1-11 – the data matrix has been revised as requested for each deficiency. The revised data matrix is attached.
- Deficiency 12 - Certification with Respect to Citation of Data – this form has been revised to checkmark the box for General Offer to Pay. The revised form is attached.
- Deficiency 13 – Source and identity of ENV503 is not adequately described.

  Envera has conducted and submitted studies that employed the most modern identification techniques that are currently available. These studies prove that ENV503 and GB03 are the same strain of *Bacillus amyloliquefaciens.* This was accepted by Dr. John Kough of BPPD in a meeting with Envera representatives and other BPPD representatives Mike Mendelsohn and Shanon Borges on September 29, 2015. A summary of that meeting is appended to MRID 50149804 along with the identification reports by Accugenix (Charles River) and NCH Agricultural Solutions. Therefore we respectfully disagree with the statement in Deficiency 13 and the need for further identification and toxicity data. If BPPD has changed its technical position provided in the 2015 meeting we request that the detailed technical basis for the change be provided so that we can review it.

ENV503 Biofungicide Wettable Powder - 87645-U

- Data matrix deficiencies 1-4 – the data matrix has been revised as requested for each deficiency. The revised data matrix is attached.
- Label – sub-label B for seed treatments has been added to this label. Also the respirator language has been revised as requested. A revised label is attached.

- EPA Form 8570-1 – the application form has been revised to include additional package types and sizes as requested. A revised application form is attached.

If you need to contact me regarding this submission I can be reached at the telephone number and email address listed below. Thank you for your assistance with this application.

Sincerely,

James M. Wagner
Agent for Envera LLC
Telephone: (302) 635-7290; Email: james@wagnerreg.com

Enclosures

Boukedes, Alexandra

From: Boukedes, Alexandra
Sent: Wednesday, August 9, 2017 1:29 PM
To: 'James Wagner'
Cc: Kausch, Jeannine; Tom Hashman; Michael Matheny
Subject: RE: ENV503 - 87645-G, -U - Prelim Response to 75 Day Deficiency letter

Hi Jim,

Thank you for the emailed version of the preliminary response to BPPD's 75-day letter. My colleagues and I will review the response and let you know how we will proceed. Thank you for your help and please let me know if you have any further questions or concerns.

Best,
Alex Boukedes

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-347-0305
boukedes.alexandra@epa.gov

From: James Wagner [mailto:jmw@wagnerreg.com]
Sent: Wednesday, August 9, 2017 12:52 PM
To: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Cc: Kausch, Jeannine <Kausch.Jeannine@epa.gov>; Tom Hashman <thashman@envera.com>; Michael Matheny <mmatheny@envera.com>
Subject: ENV503 - 87645-G, -U - Prelim Response to 75 Day Deficiency letter

Dear Alexandra,

I am submitting the attached preliminary response to BPPD's 75 day letter for the referenced registration applications. In this letter we are requesting additional information which we view as essential for our preparation of a formal response. Please let me if you will provide the requested information and if so when we might expect to receive it. Thank you for your help with this. I have sent a hard copy of this letter by Federal Express delivery.

Thanks and regards,

Jim Wagner

Regulatory Consultant to Envera LLC
Tel: (302) 635-7290
Mobile: (302) 530-5745

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

July 13, 2017

~~**CONTAINS CONFIDENTIAL BUSINESS INFORMATION**~~

BY CERTIFIED MAIL
RETURN RECEIPT REQUESTED

James M. Wagner
Authorized Agent to Envera, LLC
Wagner Regulatory Associates, Inc.
P.O. Box 640
Hockessin, DE 19707

Subject: 75-day Deficiency: Acute Toxicity/Pathogenicity Study

Application for Registration Dated January 23, 2017
EPA Receipt Date: January 24, 2017
Product Name: ENV503 Biofungicide MUP
EPA File Symbol: 87645-G
OPP Decision Number: 526002

Application for Registration Dated January 23, 2017
EPA Receipt Date: January 24, 2017
Product Name: ENV503 Biofungicide Wettable Powder
EPA File Symbol: 87645-U
OPP Decision Number: 526004

Pesticide Petition for a Tolerance Exemption Dated January 23, 2017
EPA Receipt Date: January 24, 2017
Pesticide Petition Number: 7F8546
OPP Decision Number: 526005

Dear Mr. Wagner:

The U.S. Environmental Protection Agency (EPA or Agency) has received and begun its in-depth review of the subject applications and has determined that they are incomplete and that further information is needed. This letter is a written notification of that deficiency and identifies your options under 40 CFR § 152.105.

At this time, the EPA has identified the following deficiency in its review of the subject applications:

The EPA reviewed the minutes of the September 29, 2015, meeting that you attached as an appendix to MRID No. 501598-04, as well as its own records, and respectfully disagrees with your contention from your response to the May 10, 2017, 10-day deficiency letter that further identification and toxicity data are not needed to support these applications.

In situations, like this one, where an applicant isolates a microorganism from another company's product and aims to rely on the other company's generic data (e.g., toxicological data), the EPA generally asks that detailed product identity information and a bridging study (i.e., a toxicity/pathogenicity study done with the applicant's microorganism) be provided. The EPA recognizes that, with the previous *Bacillus amyloliquefaciens* strain ENV503 application that was rejected in 2015 (EPA File Symbol: 87645-E), it did not inform you appropriately of the need for a bridging study. We have now done so and will continue with the review of the current applications, if you submit data obtained from a toxicity/pathogenicity study (including clearance data) for acute pulmonary toxicity/pathogenicity (Guideline 885.3150) or acute injection toxicity/pathogenicity (Guideline 885.3200) using *Bacillus amyloliquefaciens* strain ENV503 as the test substance. While you have the option of conducting either toxicity/pathogenicity study, the acute injection toxicity/pathogenicity study is preferable. An acceptable toxicity/pathogenicity study (as described above), in conjunction with your product identity information, will provide confidence to the EPA that the data generated using *Bacillus subtilis* strain GB03 as the test substance and to which you cite are adequate to support your applications.

Further review of your applications and your response to the deficiency may identify additional deficiencies and you will be so informed.

In accordance with 40 CFR § 152.105, you are allowed 75 days from the date of this letter to provide a response concerning the deficiency listed in this letter. Please ensure that you consider each of the options below in determining how and when you respond to this letter. You have the following three options:

1. **Resolve the Issue.** You may resolve the issue by submitting a correction or an addition to complete the applications by September 26, 2017, or you may submit an explanation of why it will take longer than 75 days to address the deficiency. For the latter option, your explanation must include a written commitment and schedule for submitting the remaining information and/or data. When submitting information and/or data in response to this letter, a copy of this letter should accompany the submission to facilitate processing.

2. **Withdraw the Applications.** You may withdraw your applications. If fees were paid, the EPA will provide any applicable refund as soon as practicable.[1] A withdrawal concludes the EPA's review of your applications. Any subsequent submission of the same applications must then be submitted as new applications with new deadlines for the EPA to make determinations on your applications and, as applicable, subject to new registration service fees.

[1] See http://www2.epa.gov/pria-fees/overview-pria-fee-reduction-and-refund-formula for more information on refunds.

3. **Not Respond Properly.** If you do not respond to this letter by September 26, 2017, or if you respond with a date on which you expect to complete the applications but fail to meet that scheduled date, the EPA will administratively withdraw your applications. If fees were paid, the EPA will provide any applicable refund as soon as practicable.[2] A withdrawal concludes the EPA's review of your applications. Any subsequent submission of the same applications must then be submitted as new applications with new deadlines for the EPA to make determinations on your applications and, as applicable, subject to new registration service fees.

If you have any questions concerning this letter, please contact Alex Boukedes by telephone at (703) 347-0305 or via email at boukedes.alexandra@epa.gov.

Sincerely,

Jeannine Kausch, Product Manager 92
Microbial Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)
Office of Pesticide Programs

[2] See footnote #1.

Boukedes, Alexandra

From: Kausch, Jeannine
Sent: Thursday, July 13, 2017 4:41 PM
To: Boukedes, Alexandra
Subject: FW: Review Requested PRIA 75-day letter for 87645-G, U and Tolerance Petition
Attachments: B. amyloliquefaciens ENV503_87645-G, 87645-U, & 7F8546_75-day Deficiency Letter_07-13-2017.pdf

Sensitivity: Confidential

Hi Alex,

Along with this email correspondence, please ensure that you put the delegation email from ShaRon into the jacket. (I think she sent it yesterday.) Also, there is a 75-day letter tab that needs to be filled in for all the applications. I can show you how to do this next week, or you can maybe ask Nicola (if she is in the office) tomorrow. I showed her how to enter this information previously.

Thanks!
Jeannine

From: Reynolds, Alan
Sent: Thursday, July 13, 2017 3:39 PM
To: Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Cc: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Subject: RE: Review Requested PRIA 75-day letter for 87645-G, U and Tolerance Petition
Sensitivity: Confidential

Hi Jeannine-

I concur on the 75 day letter.

Thanks, Alan

Alan Reynolds
Entomologist
Biopesticides and Pollution Prevention Division (7511P)
Office of Pesticide Programs

U.S. Environmental Protection Agency
1200 Pennsylvania Avenue NW
Washington, DC 20460
phone: (703) 605-0515
fax: (703) 308-7026

From: Kausch, Jeannine
Sent: Thursday, July 13, 2017 2:30 PM
To: Reynolds, Alan <Reynolds.Alan@epa.gov>
Cc: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Subject: FW: Review Requested PRIA 75-day letter for 87645-G, U and Tolerance Petition
Sensitivity: Confidential

Hi Alan,

Please find a 75-day deficiency letter attached for a set of applications containing the new active ingredient *Bacillus amyloliquefaciens* strain ENV503. We issued a 10-day deficiency letter for these applications, and the applicant responded to all of the rejectable deficiencies, except for the request for a bridging study. In talking with OGC about this situation, we were told that we could not reject the applications on the basis of the missing bridging study because we didn't previously tell the applicant that it needed to do this study. (This applicant previously came in with the same active ingredient in one product, and we rejected it. Unfortunately, even though the science reviewer at that time conveyed to the previous RAL that we needed a bridging study, this did not make it to the applicant.)

So, long story short (let me know if you need additional details), we still need the bridging study to move forward with the current applications according to the science reviewers. Thus, we are using the 75-day deficiency letter to hopefully get it this time.

Please review the attached letter, let me know if you have any comments/questions, and provide your concurrence when you are OK with the letter's content.

Thanks,
Jeannine

Jeannine Kausch
U.S. EPA Office of Pesticide Programs
1200 Pennsylvania Avenue NW (7511P)
Washington, DC 20460-0001
703-347-8820
kausch.jeannine@epa.gov

From: Boukedes, Alexandra
Sent: Thursday, July 13, 2017 1:23 PM
To: Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: RE: Review Requested PRIA 75-day letter for 87645-G, U and Tolerance Petition

Hi Jeannine,

The letter looks good! I accepted the track changes and attached it above. Thanks for your help!

Thanks
Alex

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-347-0305
boukedes.alexandra@epa.gov

From: Kausch, Jeannine
Sent: Thursday, July 13, 2017 12:43 PM
To: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Subject: RE: Review Requested PRIA 75-day letter for 87645-G, U and Tolerance Petition

Hi Alex,

I have reviewed and revised the 75-day deficiency letter somewhat. For the paragraphs I made major changes to (on page 2), I ran them by John (and he seemed OK with them). I wanted to explain what we typically require in situations like this, how we neglected to do that previously with this company, and how these new data will help our risk assessments.

Please review, make any additional revisions as necessary, and send back a clean copy to me when you think it is ready to send to Alan for concurrence.

Thanks,
Jeannine

[illegible]
U.S. EPA Office of Pesticide Programs
1200 Pennsylvania Avenue NW (7511P)
Washington, DC 20460-0001
703-347-0920
kausch.jeannine@epa.gov

From: Boukedes, Alexandra
Sent: Wednesday, July 05, 2017 10:40 AM
To: Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: Review Requested PRIA 75-day letter for 87645-G, U and Tolerance Petition

Hi Jeannine,

Please find attached a 75-day letter for the data deficiencies for *Bacillus amyloliquefaciens* ENV503 (EPA Reg. No. 87645-G, U, and tolerance petition). I sent the draft letter to John and Mohammed for review. Please let me know if you need anything else.

Thanks,
Alex

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency

703-347-0305
boukedes.alexandra@epa.gov

Boukedes, Alexandra

From: Carlisle, Sharon
Sent: Wednesday, July 12, 2017 12:58 PM
To: OPP BPPD MPB
Cc: McNally, Robert; Hartman, Mark; Leahy, John; Hollis, Linda; Ellis, Frank
Subject: MPB Delegation

Hello Everyone
I will be out of the office unexpectedly until Monday. Alan Reynolds and Wiebke Tapken will be acting chief on the dates provided below:

Alan Reynolds, July 12th and 13th
Wiebke Tapken, July 14th

Thanks,
ShaRon

ShaRon Carlisle
Associate Chief, Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division (7511 P)
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-308-6427
carlisle.sharon@epa.gov

Boukedes, Alexandra

From: Zuber, Mohammed
Sent: Thursday, June 8, 2017 10:41 AM
To: Boukedes, Alexandra
Cc: Kough, John
Subject: Envera 10-Day Letter Microbial ID Deficiency

Good Morning Alex: John and I have come up with the following response with regard to Deficiency #13 in our 10-Day Letter.

The Agency reviewed the minutes of the meeting (on 09/29/2015) the Registrant attached as an Appendix to a submitted study (MRID: 50159804) and also its internal meeting minutes. The Agency has concluded that it has not agreed with the Registrant's actions mentioned in the first paragraph of the Deficiency #13 (in bold below). However, the Agency will consider these actions acceptable on the condition that the Registrant will submit the required data mentioned in the second paragraph of the Deficiency #13 (in bold below).

"Deficiency #13. You purchased Companion 2-3-2 Biological Fungicide online from Extreme Web Sales, Inc. on October 2, 2012. You prepared serial dilutions of the Companion product and plated them onto solid agar plates to obtain single colonies. You used one such single colony to identify and prepare freezer stocks of this isolate as a seed strain and labeled this product ENV503. Whole genome sequencing of ENV503 confirmed its identity to be *Bacillus subtilis* strain GB03 according to the NCBI Genbank sequence. You are interested in registering ENV503 as a new active ingredient, citing existing data for GB03.

Since the source and identity of ENV503 is not adequately described in MRID Number 50159804, you are required to provide (1) additional biochemical or other identification method data to confirm the identity of the microbe as *Bacillus amyloliquefaciens* and (2) a toxicity/pathogenicity study (including clearance data) for Acute Pulmonary Toxicity/Pathogenicity (885.3150) or Acute Injection Toxicity/Pathogenicity (885.3200) using ENV503 as the test substance. While you have the option of conducting either toxicity/pathogenicity study, the Acute Injection Toxicity/Pathogenicity study is preferable."

Thank you

With Best Regards

Have a Great Day

Mohammed

Boukedes, Alexandra

From: Boukedes, Alexandra
Sent: Wednesday, May 17, 2017 2:41 PM
To: 'James Wagner'
Subject: RE: 87645-G and 87645-U 10-day Letter

Hi Mr. Wagner,

Because of the federal holiday on the 29th (Memorial Day), you will have until Wednesday May 31st to respond to the 10-day letter. Please let me know if you have any questions between now and then.

Best,
Alex Boukedes

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-347-0305
boukedes.alexandra@epa.gov

From: James Wagner [mailto:jmw@wagnerreg.com]
Sent: Wednesday, May 17, 2017 2:18 PM
To: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Subject: RE: 87645-G and 87645-U 10-day Letter

Dear Alex,

We received the letter yesterday May 16th. So we would have until May 30th to provide our response, correct?

Thanks,

Jim Wagner
Regulatory Consultant
Tel: (302) 635-7290
Mobile: (302) 530-5745

From: Boukedes, Alexandra [mailto:boukedes.alexandra@epa.gov]
Sent: Tuesday, May 16, 2017 7:57 AM

To: James Wagner <jmw@wagnerreg.com>
Subject: 87645-G and 87645-U 10-day Letter

Hello Mr. Wagner,

On Thursday May 11th I mailed to you a 10-day letter (containing confidential business information) for the products ENV503 Biofungicide MUP and ENV503 Biofungicide Wettable Powder. Please let me know when you receive this letter as this will start the 10 business day response period. Please let me know if you have any questions!

Best,
Alex Boukedes

Alexandra Boukedes
Microbial Pesticides Branch
Biopesticides and Pollution Prevention Division
Office of Pesticide Programs
U.S. Environmental Protection Agency
703-347-0305
boukedes.alexandra@epa.gov

SENDER: *COMPLETE THIS SECTION*

- Complete items 1, 2, and 3. Also complete item 4 if Restricted Delivery is desired.
- Print your name and address on the reverse so that we can return the card to you.
- Attach this card to the back of the mailpiece, or on the front if space permits.

1. Article Addressed to:

James M. Wagner
Wagner Regulatory Associates, Inc.
P.O. Box 640
Hockessin, DE
19707

COMPLETE THIS SECTION ON DELIVERY

A. Signature
X [illegible] ☐ Agent ☐ Addressee

B. Received by (*Printed Name*) Carrie Nolan
C. Date of Delivery 5/12

D. Is delivery address different from item 1? ☐ Yes
If YES, enter delivery address below: ☐ No

3. Service Type
☒ Certified Mail ☐ Express Mail
☐ Registered ☒ Return Receipt for Merchandise
☐ Insured Mail ☐ C.O.D.

4. Restricted Delivery? (*Extra Fee*) ☐ Yes

2. Article Number
(*Transfer from service label*) 7008 3230 0000 9474 4324

PS Form 3811, February 2004 Domestic Return Receipt 102595-02-M-1540

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

May 10, 2017

~~**CONTAINS CONFIDENTIAL BUSINESS INFORMATION**~~

BY CERTIFIED MAIL
RETURN RECEIPT REQUESTED

James M. Wagner
Authorized Agent to Envera, LLC
Wagner Regulatory Associates, Inc.
P.O. Box 640
Hockessin, DE 19707

Subject: 90-day Preliminary Technical Screening Results
Product Names: ENV503 Biofungicide MUP and ENV503 Biofungicide Wettable Powder
EPA File Symbols: 87645-G and 87645-U
Pesticide Petition Number: 7F8546
Application Date: January 23, 2017
OPP Decision Numbers: 526002, 526004, and 526005

Dear Mr. Wagner:

The U.S. Environmental Protection Agency (Agency or EPA) has completed its preliminary technical screening of your applications pursuant to Section 33(f)(4)(B)(i)(II) of the Federal Insecticide, Fungicide, and Rodenticide Act (FIFRA), as amended by the Pesticide Registration Improvement Extension Act (PRIA 3). The EPA has determined that your applications have not passed the preliminary technical screening and therefore are subject to rejection if the applications are not corrected.

Specifically, you must provide the data and/or information described below:

87645-G Rejectable Label Deficiencies

1. In accordance with the definitions presented in 40 CFR § 152.3, end-use and manufacturing-use pesticide products are defined as follows:

   "*End use product* means a pesticide product whose labeling (1) Includes directions for use of the product (as distributed or sold, or after combination by the user with other substances) for

controlling pests or defoliating, desiccating, or regulating the growth of plants, and (2) Does not state that the product may be used to manufacture or formulate other pesticide products."

"*Manufacturing use product* means any pesticide product that is not an end-use product."

Because sub-label B ("For Use as a Seed Treatment") meets the definition of an end-use pesticide product and because a manufacturing-use pesticide product, which 87645-G appears to be, cannot also be an end-use pesticide product, sub-label B must be removed from this label and moved to the label for 87645-U, the associated end-use pesticide product.

87645-G Rejectable Data Deficiencies

1. You must correct the representation of the Acute Dermal Toxicity (870.1200) data requirement on the data matrix. You must replace the current MRID Number for Acute Dermal Toxicity with MRID Number 41812303 and correct the submitter's name to reflect the company that is considered to be the original data submitter for the aforementioned study.

2. The "submitter" column on the data matrix reflects the company that is considered to be the original data submitter for a particular MRID Number. You must correct the submitter's name for the Acute Pulmonary Toxicity/Pathogenicity (885.3150) and Acute Injection Toxicity/Pathogenicity (885.3200) data requirements to reflect the original data submitter for these studies.

3. The information in MRID Number 50159801 only addresses toxicity and does not address pathogenicity. You must therefore adjust the information on the data matrix to reflect that only the Acute Oral Toxicity (870.1100) data requirement was covered by the aforementioned study. To address the Acute Oral Toxicity/Pathogenicity (885.3050) data requirement, you must add a separate line that cites to MRID Number 41812302 and provide the company that is considered to be the original data submitter and the appropriate status for this study.

4. You must correct the status of the study submitted for the Acute Inhalation Toxicity (870.1300) data requirement from "OLD" to "Own" and indicate that a waiver was submitted in the "Note" column on the data matrix.

5. You must correct the status of the study submitted for the Primary Dermal Irritation (870.2500) data requirement from "WAI" to "Own" and indicate that a waiver was submitted in the "Note" column on the data matrix. ("WAI" is not a choice for the status of studies, according to the instructions for EPA Form 8570-35 (Data Matrix).)

6. You must correct the representation of the Avian Oral Toxicity (885.4050) data requirement on the data matrix. You must replace the current MRID Number for Avian Oral Toxicity with MRID Number 42578301, correct the submitter's name to reflect the company that is considered to be the original data submitter for the aforementioned study, and correct the status of the MRID Number to "OLD".

7. You must indicate that a waiver was submitted in the "Note" column on the data matrix for the Avian Inhalation Toxicity/Pathogenicity (885.4100) data requirement.

8. You must include citation as to how the Wild Mammal Toxicity/Pathogenicity (885.4150) data requirement has been fulfilled on the data matrix.

9. You must correct the representation of the Freshwater Fish Toxicity/Pathogenicity (885.4200), Freshwater Invertebrate Toxicity/Pathogenicity (885.4240), Estuarine/Marine Fish and Invertebrate Testing (885.4280), and Nontarget Plant Testing (885.4300) data requirements on the data matrix. You must replace the current MRID Number for Freshwater Fish Toxicity/Pathogenicity, Freshwater Invertebrate Toxicity/Pathogenicity, Estuarine/Marine Fish and Invertebrate Testing, and Nontarget Plant Testing with MRID Number 47162302; correct the submitter's name to reflect the company that is considered to be the original data submitter for the aforementioned study; and correct the status of the MRID Number to "PAY".

10. You must correct the representation of the Nontarget Insect Testing (885.4340) data requirement on the data matrix. You must replace the current MRID Number for Nontarget Insect Testing with MRID Numbers 47162305, 47162303, and 47162304; correct the submitter's name to reflect the company that is considered to be the original data submitter for the aforementioned studies; and correct the status of the MRID Number to "PAY".

11. You must correct the representation of the Honey Bee Testing (885.4380) data requirement on the data matrix. You must replace the current MRID Number for Honey Bee Testing with MRID Number 47162306, correct the submitter's name to reflect the company that is considered to be the original data submitter for the aforementioned study, and correct the status of the MRID Number to "PAY".

12. Because some of the data cited are compensable (MRID Numbers 47162302, 47162303, 47162304, 47162305, and 47162306), you must follow the instructions and complete EPA Form 8570-34 (Certification with Respect to Citation of Data) appropriately. That is, you must check the box in Section II (General Offer to Pay) of the form. For more information on compensable data, please see the following Pesticide Registration Manual resource: Chapter 10 - Data Compensation Requirements (https://www.epa.gov/pesticide-registration/pesticide-registration-manual-chapter-10-data-compensation-requirements).

13. You purchased Companion 2-3-2 Biological Fungicide online from Extreme Web Sales, Inc. on October 2, 2012. You prepared serial dilutions of the Companion product and plated them onto solid agar plates to obtain single colonies. You used one such single colony to identify and prepare freezer stocks of this isolate as a seed strain and labeled this product ENV503. Whole genome sequencing of ENV503 confirmed its identity to be *Bacillus subtilis* strain GB03 according to the NCBI Genbank sequence. You are interested in registering ENV503 as a new active ingredient, citing existing data for GB03.

    Since the source and identity of ENV503 is not adequately described in MRID Number 50159804, you are required to provide (1) additional biochemical or other identification method data to confirm the identity of the microbe as *Bacillus amyloliquefaciens* and (2)

a toxicity/pathogenicity study (including clearance data) for Acute Pulmonary Toxicity/Pathogenicity (885.3150) or Acute Injection Toxicity/Pathogenicity (885.3200) using ENV503 as the test substance. While you have the option of conducting either toxicity/pathogenicity study, the Acute Injection Toxicity/Pathogenicity study is preferable.

87645-U Rejectable Data Deficiencies

1. You must correct the representation of the Acute Dermal Toxicity (870.1200) data requirement on the data matrix. You must replace the current MRID Number for Acute Dermal Toxicity with MRID Number 41812303, correct the submitter's name to reflect the company that is considered to be the original data submitter for the aforementioned study, and correct the status of the MRID Number to "OLD".

2. You must include citations accurately reflecting how the Acute Oral Toxicity (870.1100) and Acute Eye Irritation (870.2400) data requirements have been fulfilled on the data matrix. As it appears as though you are citing to your own data (done with 87645-G) to fulfill these data requirements, you must cite to MRID Number 50159801 (for acute oral toxicity) and MRID Number 50159802 (for acute eye irritation) and include the appropriate information in the remaining columns.

3. You must correct the status of the study submitted for the Acute Inhalation Toxicity (870.1300) and Primary Dermal Irritation (870.2500) data requirements from "WAI" to "Own" and indicate that a waiver was submitted in the "Note" column on the data matrix. ("WAI" is not a choice for the status of studies, according to the instructions for EPA Form 8570-35 (Data Matrix).)

4. For all generic (TGAI) data cited on the data matrix (e.g., acute toxicity/pathogenicity, cell culture and nontarget organism data requirements), you must make the adjustments indicated in the section directly above and make sure the corrected citations align with those on the 87645-G data matrix.

In order for the review of your pesticide products to continue, you will need to correct your applications to address the items listed above within 10 business days of the date you received this letter. The EPA must receive your corrections by the 10th business day. The EPA recommends sending your complete set of corrections by email to the contact listed below to ensure it is received in a timely manner. If studies or confidential business information are being submitted by mail, a complete courtesy copy, minus confidential information, received by email by the deadline will be considered timely. If you cannot correct the applications or do not respond within 10 business days, your applications will be rejected. At this time, you could also choose to withdraw your applications.

In addition to the deficiencies listed above, the preliminary technical screening identified the following shortcomings. Addressing these shortcomings now will improve the likelihood your applications can be granted as requested and in an efficient manner.

87645-G Shortcomings

1. Data Matrix - For all data requirements not covered in the respective rejectable section above, you must ensure that the information presented on this form (e.g., the status of each of the studies) is accurate and appropriate.

87645-U Shortcomings

1. Data Matrix - For all data requirements not covered in the respective rejectable section above, you must ensure that the information presented on this form (e.g., the status of each of the studies) is accurate and appropriate.

2. Container Sizes and Types - On EPA Form 8570-1, the container size is indicated as 500 pounds and the material is indicated as plastic. On the label, however, there are container handling instructions for 4- and 8-ounce foil packets and containers less than or equal to 50 pounds. You must clarify the container material and size on the EPA Form 8570-1 and/or correct the container handling section of the label to reflect the actual container types and sizes to be sold or distributed.

3. Respirator Language - You must update the respirator language under the Personal Protective Equipment section to the following:

   "Mixer/loaders and applicators must wear a NIOSH-approved particulate respirator with any R or P filter with NIOSH approval number prefix TC-84A; or a NIOSH-approved powered air purifying respirator with an HE filter with NIOSH approval number prefix TC-21C. Repeated exposure to high concentrations of microbial proteins can cause allergic sensitization."

If you have questions concerning this letter, please contact Alex Boukedes by telephone at (703) 347-0305 or via email at boukedes.alexandra@epa.gov.

Sincerely,

Jeannine Kausch, Product Manager 92
Microbial Pesticides Branch
Biopesticides and Pollution
Prevention Division (7511P)
Office of Pesticide Programs

Boukedes, Alexandra

From: Carlisle, Sharon
Sent: Thursday, April 13, 2017 8:35 AM
To: Kausch, Jeannine; Mendelsohn, Mike
Cc: Boukedes, Alexandra
Subject: RE: Bacillus amyloliquefaciens strain ENV503 - Follow Up to Yesterday's Discussion

Jeannine – I apologize for the delay in response.

Based on our discussion in the production meeting and your additional information provided below it seems the bridging study should be added to the deficiency section of the letter.

Alex should probably start working on the rejection letter and you should be prepared to present at the PRIA bi-weekly next week.

Thanks,

ShaRon

703-308-6427
carlisle.sharon@epa.gov

From: Kausch, Jeannine
Sent: Tuesday, April 11, 2017 11:02 AM
To: Carlisle, Sharon <Carlisle.Sharon@epa.gov>; Mendelsohn, Mike <Mendelsohn.Mike@epa.gov>
Cc: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Subject: Bacillus amyloliquefaciens strain ENV503 - Follow Up to Yesterday's Discussion
Importance: High

Hi ShaRon and Mike,

Per our discussion yesterday at the production meeting (i.e., absence of a bridging study) from the *Bacillus amyloliquefaciens* strain ENV503 applications, I took a look at the documentation for the previously rejected product. Because the applicant was unable to obtain this active ingredient from the culture collection (BASF apparently was blocking access), the applicant isolated the active ingredient from another company's product (Companion, EPA Reg. No. 71065-3, ai: *Bacillus subtilis* strain GB03). With the previously rejected product, it appears as though we asked for better product identity information (b/c of how the AI was obtained) but did not specify the need for a bridging study.

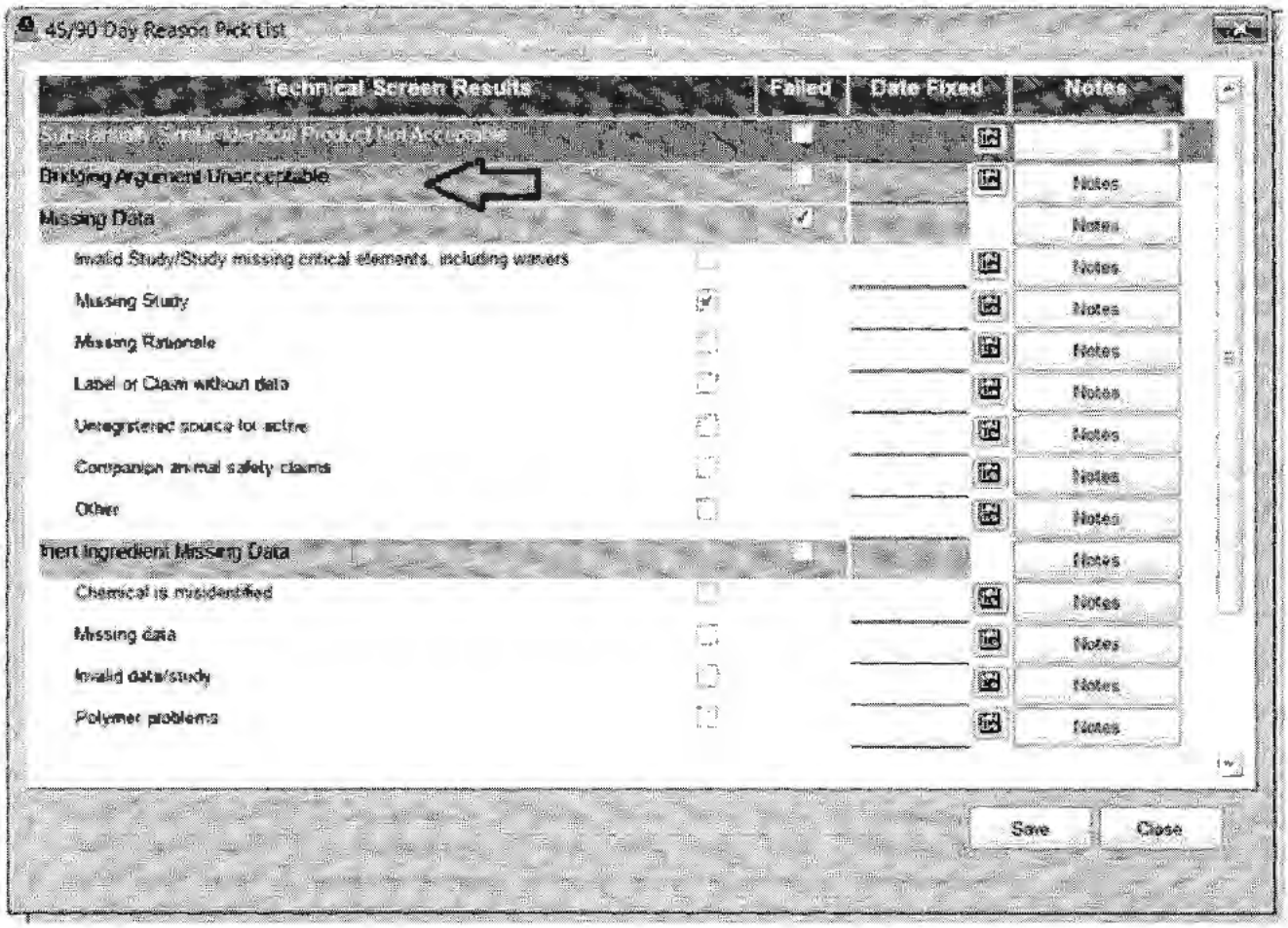
In the current situation, our scientists have indicated concern about needing a bridging study, as well as clarification as to how the applicant is making the leap from *Bacillus subtilis* to *Bacillus amyloliquefaciens*, given how the AI was obtained. Here's an excerpt from the draft 10-day deficiency letter (re: this issue):

"You purchased Companion 2-3-2 Biological Fungicide online from Extreme Web Sales, Inc. on October 2, 2012. You prepared serial dilutions of the Companion product and plated them onto solid agar plates to obtain single colonies. You used one such single colony to identify and prepare freezer stocks of this isolate as a seed strain and labeled this product ENV503. Whole genome sequencing of ENV503 confirmed its identity to be *Bacillus subtilis* strain GB03 according to the

NCBI Genbank sequence. You are interested in registering ENV503 as a new active ingredient, citing existing data for GB03.

Since the source and identity of ENV503 is not adequately described in MRID Number 50159804, you are required to provide (1) additional biochemical or other identification method data to confirm the identity of the microbe as *Bacillus amyloliquefaciens* and (2) a toxicity/pathogenicity study (including clearance data) for Acute Pulmonary Toxicity/Pathogenicity (885.3150) or Acute Injection Toxicity/Pathogenicity (885.3200) using ENV503 as the test substance. While you have the option of conducting either study, the Acute Injection Toxicity/Pathogenicity study is preferable."

To the best of my knowledge, it has been a standard to ask for a bridging study for situations like this, although it appears that we did not relay this to this applicant with the previously rejected product. Having said that, it does look like an unacceptable bridging argument is a rejectable issue (see below from OPPIN):



As I am in the process of reviewing the 10-day deficiency letter from Alex Boukedes, please let me know whether you would like me to put this particular issue in the rejectable section or shortcoming (non-rejectable) section of the 10-day deficiency letter.

To me, even if these applications pass the preliminary technical screening (if we make the need for a tox/path study a non-rejectable issue), we would be waiting on the applicant to submit the study and wouldn't be able to move forward with the science review. This seems to fly in the face of the intent of the preliminary technical screening, which is outlined in the statute and here (in the grey box): https://www.epa.gov/pria-fees/checklists-4590-preliminary-technical-screen.

Thanks,

Boukedes, Alexandra

From: Zuber, Mohammed
Sent: Tuesday, March 28, 2017 9:28 AM
To: Kough, John; Boukedes, Alexandra
Cc: Kausch, Jeannine
Subject: RE: ENV503 - Identity of the Active Ingredient

Good Morning John: Thank you for looking into this draft 10 day letter and addressing Alex's questions.

Alex: I have no other comments.

Thank you

With Best Regards

Have a Great Day

Mohammed

From: Kough, John
Sent: Tuesday, March 28, 2017 9:23 AM
To: Boukedes, Alexandra <boukedes.alexandra@epa.gov>; Zuber, Mohammed <Zuber.Mohammed@epa.gov>
Cc: Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: RE: ENV503 - Identity of the Active Ingredient

Alex,

I will let Mohammed answer your questions too but I think the parenthetical question is that ENV503 is not adequately addressed as to source and ID. The second highlight is not a requirement but a suggestion. If you feel that is not needed (we already said "either or" earlier in the section), then you can remove the phrase. Otherwise the letter looks good enough for Jeannine to look at.

John K.

From: Boukedes, Alexandra
Sent: Tuesday, March 28, 2017 9:08 AM
To: Zuber, Mohammed <Zuber.Mohammed@epa.gov>
Cc: Kough, John <Kough.John@epa.gov>; Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: RE: ENV503 - Identity of the Active Ingredient

Hello Mohammed and John,

I added the updated science language to the 10-day letter. I have one question which is highlighted in the text of the letter. Along with clarification of my question, I am hoping you can take a quick look and make sure the science language is correct (I don't think I changed it, at least not too much). I appreciate all your time and help!

Thanks,
Alex

From: Zuber, Mohammed
Sent: Monday, March 27, 2017 2:11 PM
To: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Cc: Kough, John <Kough.John@epa.gov>; Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: FW: ENV503 - Identity of the Active Ingredient

Hi Alex: Since our meeting this morning, we investigated In detail the identity of ENV503. Please look at the language in bold below that John and I have come up with regard to the deficiencies in the case of ENV503.

Please me know if you have any further questions, and if I can be of any additional help.

Thank you

With Best Regards

Mohammed

From: Kough, John
Sent: Monday, March 27, 2017 1:55 PM
To: Zuber, Mohammed <Zuber.Mohammed@epa.gov>
Subject: RE: ENV503 - Identity of the Active Ingredient

Thanks Mohammed. This is great: very thorough. I have a few suggestions for the 10-day letter in yellow highlight. I think we just need to point out the name change between sequence and their product and request the biochemical test results or other ID methods that confirm GB03 as *B. amyloliquefaciens*.

John K.

From: Zuber, Mohammed
Sent: Monday, March 27, 2017 12:19 PM
To: Kough, John <Kough.John@epa.gov>
Subject: ENV503 - Identity of the Active Ingredient

Hi John: I looked into this issue of sequence identity between ENV503 and GB03. Here is what I found:

ENV503 (aka Bacillus amyloliquefaciens according to the Registrant) bacterial strain was subjected to Whole Genome Sequencing.
Whole Genome Sequencing confirmed the identity of ENV503 as GB03.
GB03 Whole Genome Sequence is published (Choi et al., 2014) – PDF Attached.

Choi et al (2014) referred to this strain as Bacillus amyloliquefaciens GB03 in this publication.
In GenBank Sequence Databases (PDFs attached), this strain is referred to as Bacillus subtilis GB03.
In summary, Bacillus amyloliquefaciens strain GB03, Bacillus amyloliquefaciens strain ENV503 and Bacillus subtilis strain GB03 are One and the Same.

For the 10 Day Letter, I am thinking of the following language:

The Registrant purchased the Companion 2-3-2 Biological Fungicide online from Extreme Web Sales, Inc. on 10/02/2012.
The Registrant prepared serial dilutions of this Companion Product, and plated them onto solid agar plates to obtain single colonies.

The Registrant used one such single colony to identify and prepared freezer stocks of this isolate as a seed strain, and labelled this product as ENV503.
Whole Genome Sequencing of ENV503 confirmed its identity to be *Bacillus subtilis* strain GB03 according to the NCBI Genbank sequence.
The Registrant is interested in Registering ENV503 as a New Active Ingredient citing all the existing data for GB03.
However, Registration for *Bacillus subtilis* strain GB03 was cancelled by the EPA in 2014 (?, subject to clarification by the RAL). (Don't know if this is directly relevant but maybe Envera should know this fact)

Since the source and identity of the Microbe is not adequately described in the MRID 50159804, the Registrant is required to provide (1) additional biochemical or other identification method data to confirm the identity of the microbe as *Bacillus amyloliquefaciens*, and (2) a toxicity study (including clearance data) for Acute Pulmonary Toxicity (885.3150) or Acute Injection Toxicity (885.3200) studies using ENV503 as the test substance.
In the event of the failure to provide the required data within 10 business days, the Agency is recommending withdrawal of this Registration Application for this Active Ingredient.

Please edit as you feel necessary.

Thank you

With Best Regards

Mohammed

Boukedes, Alexandra

From: Zuber, Mohammed
Sent: Tuesday, March 21, 2017 11:45 AM
To: Boukedes, Alexandra
Cc: Kough, John
Subject: FW: ENV503 MUP - Rationale for Rejection

Hi Alex: Following in BOLD is the Rationale for our Rejection, that John and I came up with.

Please let me know if I can be of any additional help.

John: Thank you for your excellent feedback on my rejection language.

Thank you

With Best Regards

Mohammed

The Registrant purchased GROWTH PRODUCTS COMPANION 2-3-2 BIOLOGICA FUNGICIDE online from EXTREME WEB SALES, Inc.
The Registrant plated serial dilutions of the Companion Product to obtain Single Colonies.
The Registrant picked One Colony, prepared Freezer Stocks, and designated this as ENV503.
Whole Genome Sequencing was performed to confirm the identity of ENV503 as GB03.
The Registrant submitted data only on Acute Oral Toxicity and Acute Eye Irritation using ENV503.
RATIONALE:

(1) Description of the Source of the Microbe is not Adequate.
(2) The Agency strongly feels that obtaining the original isolate from the web rather than through normal environmental isolation makes a few extra steps/studies necessary to confirm the safety.
(3) Therefore, the Registrant is required to provide data (including clearance data) on Acute Pulmonary Toxicity (885.3150) or Acute Injection Toxicity (885.3200) using ENV503, in order to be able to bridge to 1992 Data for GB03.

details of source of microbe (history

From: Kough, John
Sent: Tuesday, March 21, 2017 11:30 AM
To: Zuber, Mohammed <Zuber.Mohammed@epa.gov>
Subject: RE: ENV503 MUP - Rationale for Rejection

Mohammed,

This looks like a reasonable explanation. I think we need to stress that obtaining the original isolate from the web rather than through normal environmental isolation makes a few extra steps/studies necessary to confirm the safety.

While not part of the rationale for why we are asking for these infectivity studies, it is important that you understand that this is less than a typical suite of safety studies for a new A.I. Also we are trying figure out if this is isolation from an existing product is a legal action and also to discourage registrants from going this route.

John K.

From: Zuber, Mohammed
Sent: Monday, March 20, 2017 11:25 AM
To: Kough, John <Kough.John@epa.gov>
Subject: ENV503 MUP - Rationale for Rejection

Hi John: Alex, the RAL on this project, has requested for our rationale for rejecting this new a.i.
So, I have written this following rationale. Please edit as you feel necessary.

The Registrant purchased GROWTH PRODUCTS COMPANION 2-3-2 BIOLOGICA FUNGICIDE online from EXTREME WEB SALES, Inc.
The Registrant plated serial dilutions of the Companion Product to obtain Single Colonies.
The Registrant picked One Colony, prepared Freezer Stocks, and designated this as ENV503.
Whole Genome Sequencing was performed to confirm the identity of ENV503 as GB03.
The Registrant submitted data only on Acute Oral Toxicity and Acute Eye Irritation using ENV503.
RATIONALE:
(1) Description of the Source of the Microbe is not Adequate.
(2) The Registrant is required to provide data (including clearance data) on Acute Pulmonary Toxicity (885.3150) or Acute Injection Toxicity (885.3200) using ENV503, in order to be able to bridge to 1992 Data for GB03.

I would greatly appreciate your feedback at your convenience.

Thank you

With Best Regards

Mohammed

Boukedes, Alexandra

From: Kausch, Jeannine
Sent: Friday, March 10, 2017 9:44 AM
To: Boukedes, Alexandra
Subject: RE: a question about MRID 49539103 for 87645-G
Attachments: FW: Texas Corn Producers Board Experimental Use Permit (EPA EUP No. 91163-EUP-1) - Issued August 25, 2016 / Final Rule for Tolerance Exemptions - Signed August 30, 2016; Bacillus subtilis Final Registration Review Decision.pdf

Hi Alex,

Thanks for bringing this to my attention as I didn't realize it might be a potential issue! I think it would be a good idea for you and I to meet about this before we have the group meeting on Wednesday. I'd like to walk you through how to ascertain whether data are compensable or exclusive use and also what would need to be fixed on the data matrices (and possibly in other forms) by the applicant to meet data compensation obligations. The applicant can't just cite to publicly available EPA documents in its data packages and satisfy data compensation requirements. It looks like the applicant cited to information from one of our registration review documents without mentioning most of those data in that registration review document on the data matrices (from what I recall). For your reference, I've attached the registration review document that I believe the applicant is citing to. Any MRID Numbers in this document (see pages 73-78) that the applicant is relying on need to be on the data matrices. Also, any other appropriate data compensation forms will need to be properly filled out. All of these items (re: data compensation issues) would be rejectable things to go into a 10-day deficiency letter. I had a situation like this last year and am attaching my email to the registrant's agent for your reference (see highlighted text in email).

Thanks again and looking forward to talking with you about this next week. Another exciting situation!

Jeannine

From: Boukedes, Alexandra
Sent: Friday, March 10, 2017 7:37 AM
To: Kausch, Jeannine <Kausch.Jeannine@epa.gov>
Subject: FW: a question about MRID 49539103 for 87645-G

HI Jeannine,

Here is the email between Sarah and Shannon about whether Evera (reg number 87645-G and 87645-U) can cite to another company's ECO data.

Thanks,
Alex

From: Butler, Sarah
Sent: Thursday, March 9, 2017 12:41 PM
To: Boukedes, Alexandra <boukedes.alexandra@epa.gov>
Subject: FW: a question about MRID 49539103 for 87645-G

Hi Alex,

Thank you for sending me the checklist. The email Shannon sent me mentioning "exclusive use" and "compensable" restrictions is below.

I'm going to go to the kitchen for lunch in about five minutes. See you over there!

From: Borges, Shannon
Sent: Wednesday, March 8, 2017 2:59 PM
To: Butler, Sarah <butler.sarah@epa.gov>; Djurickovic, Milutin <Djurickovic.Milutin@epa.gov>
Subject: RE: a question about MRID 49539103 for 87645-G

Hi Sarah,

Not sure if you got the previous version of my response (I think the attachment was too big to send). Below was my response to your email. This time I include a link instead of the document itself.

Shannon

****
Well, well...the plot thickened quickly on this one! Very good question.

It sounds like Bacillus subtilis ENV503 (a new a.i.) was isolated from an existing product containing Bacillus subtilis GB03. Products containing Bacillus subtilis GB03 are owned by another company, so Envera purchased the other company's product, isolated their a.i. from it, and are now calling it their own by a different name.

They can actually do this, but they have to give it a unique strain identifier (as they have – ENV503) and it must be considered a new a.i., which it is. As long as they can show that their strain is identical to the one they're claiming it is identical to, then they can cite to data submitted by the other company on their a.i. The catch is that the data cannot be under "exclusive use" or "compensable" restrictions. When a company submits data on a product, there is a period (10-15 years) during which only they can use the data unless they give permission to another company to use it. The data are also considered compensable, in that the company owning the data can require a payment to use the data. For our purposes, if it is under exclusive use restrictions, we have to see that the company has given permission to use the data. If the data are just compensable, we have to see proof that the applicant company offered to pay the company that owns the data for use of the data. After 15 years, though, the data are available for anyone to use. Given that Bacillus subtilis went through registration review (2010 I think), I think the data on strain GB03 are available for them to cite to. So the hurdle they have to get over is whether strain ENV503 is identical to strain GB03. That is something that should be covered in the product characterization data, and the reviewer of those data would make that determination.

Here is a link to the final decision document is attached and it describes the eco data for GB03 (https://www.regulations.gov/document?D=EPA-HQ-OPP-2007-1026-0030, see pages 31-33). This doesn't mean that we don't need an eco risk assessment, but it could mean that you don't have any data to review. As long as ENV503 and GB03 are the same thing, for the screen, you'll just need to make sure that you have all the data you need with citation to the GB03 data. For Reg Review, we determined that the data set was complete for GB03 given the uses, so unless there is anything associated with the new product that might increase exposure or risk to nontargets that would not be

covered by the available data, then the data should be complete for ENV503. Of course, that all depends on whether it really is the same thing.

Please let me know if you have any other questions or want to talk about this further.

Shannon

From: Butler, Sarah
Sent: Wednesday, March 08, 2017 11:48 AM
To: Borges, Shannon <Borges.Shannon@epa.gov>; Djurickovic, Milutin <Djurickovic.Milutin@epa.gov>
Subject: a question about MRID 49539103 for 87645-G

Hi Shannon and Milutin,

I have a question about the MRID associated with 87645-G (my new assignment).

The introduction of this document states,

"The pure culture of ENV503 MPCA (Bacillus subtilis strain ENV503) was isolated from Bacillus subtilis strain GB03 (PC Code 129068). Since ENV503 MPCA was isolated and grown from existing cultures of GB03, Envera requests that the Agency bridge from existing Tier I nontarget organisms and environmental fate studies and results for GB03 to Envera's product… Envera requests that the Agency rely on studies conducted and submitted for B. subtilis strain GB03 to satisfy the nontarget organisms and environmental fate data requirements for the registration of ENV503 Biofungicide MUP. The results of these studies are presented below.".

I do not know enough about these microorganisms to know if this is a reasonable request. Should I just go ahead and review the studies for B. subtilis strain GB03 as though they were conducted specifically for Bacillus subtilis strain ENV503?

Milutin, perhaps we can talk about this when we meet later this afternoon.

Thank you for your help!

21-Day Screen Completed by Contractor

21-Day Expires on 2-14-17

Jacket # 7F8546
MRID# _____

Content Screen: Recommend to Pass/Fail

11-3 Review: Pass/Fail/NA

Overall Status: Recommend to Pass/Fail

Transfer This Jacket to:

JEANNINE KAUSCH

PRIA 3 – 21 Day Content Screen Review Worksheet

(EPA/OPP Use Only)

September 2012

21 Day Screen Start Date: 1-24-17

Experts In-Processing Signature: B.B. Date 2-13-17 Fee Paid: Yes __

Division management contacted on issues No_____ Yes _____ Date _____

EPA Reg. Number: 7F8546	EPA Receipt Date: 1-24-17

	Items for Review			Yes	No	N/A*
1	**Application Form** (EPA Form 8570-1) signed & complete including package type					X
2	**Confidential Statement of Formula** all boxes completed, form signed, and dated (EPA Form 8570-4)					X
	a) All inerts, including fragrances, approved for the proposed uses (see Footnote A) No Inert to Review	yes	no			
3	**Certification with Respect to Citation of Data** (EPA Form 8570-34) completed and signed (N/A if 100% repack)					X
	Certificate and data matrix consistent					
	If applicant is relying on data that are compensable, is the offer to pay statement included. (see Footnote B)	yes	no			
	If applicable, is there a letter of Authorization for exclusive use only.					
4	**Formulator's Exemption Statement** (EPA Form 8570-27) completed and signed (N/A if source is unregistered or applicant owns the technical)					X
5	**Data Matrix** (EPA Form 8570-35) both internal and external copies (PR 98-5) completed and signed (N/A if 100% repack)					X
	a) Selective Method (Fee category experts use)	yes	no			
	b) Cite-All (Fee category experts use)					
	c) Applicant owns all data (Fee category experts use)					
6	**5 Copies of Label (Electronic labels on CD are encouraged and guidance is available)**			X		
7	**Is the data package consistent with PR Notice 86-5**					X
8	**Notice of Filing included with petitions**			X		

9	**If applicable for conventional applications, <u>reduced risk rationale</u>**			X
10	**<u>Required Data</u> and/or data waivers. See Footnote C.**			
	a) List study (or studies) not included with application			

Comments:

Related: 87645-G
87645-U

Documentation (Pass) or Fail
- All Required Forms Complete

Inerts (Pass) or Fail
- No Inerts to Review

PRN 11-03 (Pass) or Fail
- No Studies Submitted

2/15/17

Overall Status (Pass) or Fail

* N/A – Not Applicable

Footnotes

A. During the 21 day initial content review, all CSFs will be reviewed to determine whether all inerts listed, including fragrances, are approved for the proposed uses or have an application pending with the Agency. If an unapproved inert with no application pending with the Agency is identified, the applicant must either 1) resolve the inert issue by, for example, removing the inert, substituting it with an approved inert, submitting documentation that EPA approved the inert for the proposed pesticidal uses, correcting mistakes on the CSF, etc. or 2) provide the data to support OPP approval of the inert or 3) withdraw the application. Removing or substituting an inert ingredient will require a new CSF and may require submission of data. All information, forms, data and documentation resolving the inert issue must have been received by the Agency or the application withdrawn within the 21 day period, otherwise, the Agency will reject the application as described below.

To successfully complete this aspect of the 21 day initial content screen, applicants are **strongly encouraged** to verify that all inert ingredients have been approved for the application's uses or have an application pending with the Agency **even if a product is currently registered** by consulting the inert Web site and if the inert is not approved nor has an application pending with the Agency, to **obtain the necessary inert approval prior to submitting an application to register a pesticide product containing that inert ingredient.** Some inert ingredients are no longer approved for food uses or certain types of uses. The name and/or CAS number on a CSF must match the name and CAS number on this web site. Simple typographical errors in the name or CAS number have resulted in processing delays.

If an inert is not listed on the inert ingredient web site and the applicant believes that the inert has been approved, the applicant should contact the Inert Ingredient Assessment Branch (IIAB) at inertsbranch@epa.gov and resolve the issue. Copies of the correspondence with IIAB resolving the issue should accompany the application. All new inerts except PIP inerts are reviewed by IIAB. The IIAB should also be contacted for any questions on what supporting data needs to be submitted for and the Agency's inert review process. Questions on PIP inerts should be directed to the Chief of Microbial Pesticides Branch.

When a brand, trade, or proprietary name of an inert ingredient is listed on a CSF, additional information such as an alternate name of the inert, CAS number or other information must also be included to enable the Agency to determine if it has been approved. Each component of an inert mixture (including a fragrance) must be identified. In some cases, the supplier of the mixture or fragrance may need to provide this information to the Agency. Prior to the Agency's receipt of an application, applicants must arrange with a proprietary mixture or fragrance supplier to provide the component information to the Agency or promptly upon EPA's request. If the inert ingredients in a proprietary blend (including fragrances) cannot or are not identified or provided within the 21-day content review period, the Agency will reject the application.

During the 21 day content review, applicants should submit information to the individual identified by the Agency when the applicant is informed of an unapproved inert.

Unapproved Inerts Identified on CSFs

All applications except conventional new products and PIPs

Once an unapproved inert is identified on a CSF, the Agency will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Provide the required information necessary to identify an inert approval application that is pending with the Agency; or

3. Submit the information and data needed for the Agency to approve the unapproved inert. If this option is selected and implemented, the Agency may request an extension in the PRIA decision review timeframe to accommodate the inert review/approval process;

4. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of these options is selected and implemented by the applicant within the 21 day content review period, the Agency will reject the application and retain 25% of the full fee of the category identified.

Conventional New Product Applications

When the Registration Division identifies an unapproved inert on a CSF with an application for a new product that the applicant has not identified as requiring an inert approval (R300 or R301), it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the inert's identity or CAS number, providing documentation that the inert has been approved, or removing the unapproved inert from the CSF or replacing it with one that is approved for the application's uses; or

2. Submit the information and data needed for the Agency to approve the unapproved inert, including any required petition to establish or amend a tolerance or exemption from a tolerance. (This option may change the PRIA category for the application, which could require a longer decision review time and a larger fee. If additional fees are due, they must be received by the Agency within the 21 day content review period.)

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21-day content-review period, the Agency will reject the application and retain 25% of the appropriate fee for the new product-inert approval category.

PIP Applications

When the Biopesticide and Pollution Prevention Division identifies an unapproved inert on a PIP CSF and a request to approve the inert does not accompany the application, it will contact the applicant with the following options:

1. Correct the application by, for instance, correcting the spelling or name of the inert to that in 40 CFR 174, or providing documentation that the inert has been approved; or

2. Submit the information and data needed for the Agency to approve the unapproved inert. If an inert ingredient tolerance exemption petition is required, the petition must be received by the Agency and the B903 fee paid within the 21 day period. If this option is selected and implemented, the Agency will discuss harmonizing the timeframe for both actions.

3. Withdraw the application (the Agency retains 25% of the full fee for the fee category estimated); or

If none of the above options is selected and implemented during the 21 day content review period, the Agency will reject the application and retain 25% of the fee.

B. A policy on documentation of offers to pay is still being developed, however, for a me-too or fast track (similar/identical) new product, R300 or A530, an application without the necessary authorizations of offers to pay will be placed into either R301 or A531. The Agency recommends that authorizations of offers to pay be submitted with other PRIA applications to avoid delays in the Agency's decision.

C. Biopesticide applicants are advised to contact the Agency and discuss study waivers prior to submitting their application to the Agency. Documentation of such discussions should be submitted with the study waiver.

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

February 10, 2017

OFFICE OF CHEMICAL SAFETY
AND POLLUTION PREVENTION

OPP Decision Number: D-526005
EPA File Symbol or Registration Number: 7F8546
Description: Tolerance Petition for *Bacillus amyloliquefaciens* strain ENV503
EPA Receipt Date: 24-Jan-2017
EPA Company Number: 87645
Company Name: ENVERA, LLC

JAMES M. WAGNER
WAGNER REGULATORY ASSOCIATES, INC.
AGENT FOR ENVERA, LLC
PO BOX 640
HOCKESSIN, DE 19707-

SUBJECT: Receipt of Tolerance Petition Subject to Registration Service Fee

Dear Registrant:

The Office of Pesticide Programs has received your tolerance petition. If you submitted data with this petition, the results of the PRN-2011-3 screen will be communicated separately. During the administrative screen, the Office of Pesticide Programs has determined that this Action is subject to a Pesticide Registration Service Fee as defined in the Pesticide Registration Improvement Act.

The Action has been identified as Action Code: B590

NEW AI;FOOD USE;MICROBIAL/BIOCHEMICAL;PETITION TO ESTABLISH A TOLERANCE EXEMPTION;NO FEE: ASSOCIATED WITH ANOTHER PRIA ACTION;

No additional payment is due at this time. If you have any questions, please contact the Pesticide Registration Service Fee Ombudsman at (703)-305-5659.

Sincerely,

Front End Processing Staff
Information Technology & Resources Management Division

Fee for Service {998077T~

This package includes the following

- ◉ New Registration
- ○ Amendment

☐ Studies? ☐ Fee Waiver?

☐ volpay % Reduction: ___

for Division

- ○ AD
- ◉ BPPD
- ○ RD

Risk Mgr. ~~91~~ 92

Receipt No. S-	998077
EPA File Symbol/Reg. No.	7F8546
Pin-Punch Date:	1/24/2017

☐ This item is NOT subject to FFS action.

Action Code:

Requested: B590.0

Granted: B590.0

Amount Due: $ —

Parent/Child Decisions:

CHILD TO 87645-6

▣ Inert Cleared for Intended Use ▣ Uncleared Inert in Product

Reviewer: JENNINE KNIGHT Date: 01/30/2017

Remarks: TOLERANCE EXEMPTION PETITION (NEW AI)

*NOTE: THE PM TEAM SHOULD BE "92" INSTEAD OF "91".

EPA BIOPESTICIDES AND POLLUTION PREVENTION DIVISION COMPANY NOTICE OF FILING FOR PESTICIDE PETITIONS PUBLISHED IN THE FEDERAL REGISTER

EPA Biopesticides and Pollution Prevention Division contact:

SUBMISSION: **Email the completed template to: hollis.linda@epa.gov.**

TEMPLATE:

Envera, LLC, 220 Garfield Avenue, West Chester, Pennsylvania 19380

[Insert petition number]

EPA has received a pesticide petition ([insert petition number]) from Envera, LLC, 220 Garfield Avenue, West Chester, Pennsylvania 19380 requesting, pursuant to section 408(d) of the Federal Food, Drug, and Cosmetic Act (FFDCA), 21 U.S.C. 346a(d), to amend 40 CFR part 180 to establish an exemption from the requirement of a tolerance for residues of the microbial pesticide *Bacillus amyloliquefaciens* strain ENV503 in or on all agricultural commodities.

Pursuant to section 408(d)(2)(A)(i) of FFDCA, as amended, Envera, LLC has submitted the following summary of information, data, and arguments in support of their pesticide petition. This summary was prepared by Envera, LLC and EPA has not fully evaluated the merits of the pesticide petition. The summary may have been edited by EPA if the terminology used was unclear, the summary contained extraneous material, or the summary unintentionally made the reader conclude that the findings reflected EPA's position and not the position of the petitioner.

I. Envera, LLC Petition Summary

[Insert petition number]

A. Product Name and Proposed Use Practices

Bacillus amyloliquefaciens strain ENV503 microbial pest control product is a broad-spectrum preventative biofungicide for control or suppression of fungal and bacterial plant diseases. The product contains a naturally occurring strain of the beneficial rhizobacterium *Bacillus amyloliquefaciens*, which colonizes leaves, roots, and other plant surfaces, killing pathogenic organisms by means of antibiotic compounds (iturins) which disrupt pathogen cell wall production. *Bacillus amyloliquefaciens* rapidly colonizes plant

root hairs, leaves, and other surfaces, preventing establishment of disease-causing fungi and bacteria.

B. Product Identity/Chemistry

1. *Identity of the pesticide and corresponding residues.*

Bacillus amyloliquefaciens (spp.) is a rod shaped, Gram-positive, catalase-positive bacterium commonly found in soil. *Bacillus amyloliquefaciens* has the ability to form a tough, protective endospore, allowing the organism to tolerate extreme environmental conditions.

Bacillus amyloliquefaciens was previously classified as *Bacillus subtilis* var. *amyloliquefaciens.* Both species names are used interchangeably throughout this document.

Bacillus amyloliquefaciens MPCA is manufactured by growing *Bacillus amyloliquefaciens* strain ENV503. This strain was isolated from existing cultures of *Bacillus subtilis*. The culture was fermented under aeration in liquid culture medium until sporulation is completed. The culture is deposited at National Center for Agricultural Utilization Research in Peoria, Illinois with the accession number is NRRL B-59994.

Bacillus amyloliquefaciens spp. are not considered to be a human pathogen. *Bacillus amyloliquefaciens* produces proteolytic enzymes and is widely used as an additive in laundry detergents. *Bacillus amyloliquefaciens* is used as a soil inoculant in horticulture and agriculture.

2. *Magnitude of residues at the time of harvest and method used to determine the residue.*

Bacillus amyloliquefaciens is ubiquitous in the environment, especially in soils and agricultural environments. As a result, dietary exposure to background levels of the naturally occurring microbe likely is already occurring and likely will continue to occur. Because of its ubiquitous presence in the environment, no increase in exposure to *Bacillus amyloliquefaciens* resulting from the existing and proposed pesticidal uses when compared to existing exposure to background levels of *Bacillus amyloliquefaciens* is expected to occur.

Any potentially occurring residual deposits on crops will not harm humans because

Bacillus amyloliquefaciens strains show no toxicity, infectivity, or pathogenicity in appropriate tests.

3. *A statement of why an analytical method of detecting and measuring the levels of the pesticide residue are not needed.*

The acute toxicity studies discussed in Section C of this document are sufficient to show that there are no foreseeable human or domestic animal health hazards likely to arise from the use of the product as proposed. Envera, LLC is requesting an exemption from the requirement for a tolerance for any residues remaining in/on all agricultural commodities from pre-and post-harvest applications. Since enforcement of residue levels would not be needed, an enforcement analytical method is not required.

C. Mammalian Toxicological Profile

Toxicological data on multiple strains of *Bacillus amyloliquefaciens* have been submitted to EPA to support existing exemptions from the requirement of a tolerance for residues resulting from use in or on all agricultural crops.

Data generated using the test substance ENV503 Biofungicide MUP (*Bacillus amyloliquefaciens* strain ENV503) includes the following:

Test substance ENV503 MUP was evaluated for acute oral toxicity potential in female albino rats when administered as a gavage dose at 5000 mg/kg. The study was terminated following stopping rules of this procedure. No mortality occurred during the study. There were no clinical signs of toxicity during the study. Animals exhibited weekly weight gain, except for one that lost weight between Days 7 and 14. Gross necropsy conducted at terminal sacrifice revealed no observable abnormalities. The test substance acute oral LD50, indicated by the data, was determined to be greater than 5000 mg/kg.

An acute eye irritation study was conducted on three albino rabbits using test substance ENV503 MUP. Test substance, 100 mg, was placed into the conjunctival sac of the right eye of each animal selected for testing. All treated eyes were washed with room temperature deionized (DI) water for one minute after recording the 24-hour observation. There were no positive effects exhibited in any eyes after treatment. Therefore, the test substance is assigned Toxicity Category IV. Per Legend B, the test substance is rated minimally irritating.

Previously submitted data for a genetically identical strain of *Bacillus amyloliquefaciens* include the following:

An acceptable acute oral toxicity/ pathogenicity study performed in rats demonstrated the lack of mammalian toxicity at high levels of exposure to *Bacillus subtilis*. In this study, *Bacillus subtilis* was not toxic, infective nor pathogenic to rats given an oral dose of 1.9 x 10^8 colony forming units (CFU) per animal.

An acceptable acute pulmonary toxicity/pathogenicity study in rats demonstrated that *Bacillus subtilis* was neither toxic, pathogenic nor infective to rats dosed intratracheally with 2.84 x 10^8 CFU of the test material.

An acceptable acute intravenous injection toxicity/pathogenicity study in rats demonstrated that *Bacillus subtilis* was neither toxic, pathogenic nor infective to rats dosed intravenously with approximately 1.8 x 10^7 CFU of the test material. Although the microbe was detected in every organ tested, the test material displayed a distinct pattern of clearance.

An acceptable acute dermal toxicity study in rabbits demonstrated that *Bacillus subtilis* is not toxic when a single 2 gram (3.6 x 10^{10} CFU)/animal dose was administered dermally. Moderate signs of dermal irritation were observed but were diminished by day 15. Based on these results the test material was not considered toxic by dermal route but is expected to be moderately irritating to skin.

Envera, LLC has not observed any hypersensitivity occurrences among its employees working with strain ENV503 and concludes that it is not a dermal sensitizer.

D. Aggregate Exposure

1. *Dietary exposure.*

i. *Food.*

Bacillus amyloliquefaciens is ubiquitous in the environment, especially in soils and agricultural environments. As a result, dietary exposure to background levels of the naturally occurring microbe likely is already occurring and likely will continue to occur. Because of its ubiquitous presence in the environment, no increase in exposure to *Bacillus amyloliquefaciens* resulting from the existing and proposed pesticidal uses is expected when compared to existing exposure to background levels of *Bacillus amyloliquefaciens*.

As discussed above, dietary exposure to the naturally occurring microbe likely is already occurring and likely will continue to occur. Notably, similar *Bacillus subtilis* strains are used internationally in the production of food grade products and in fermented foods in Japan and Thailand. Reports in the literature implicating *Bacillus subtilis* in food-borne

illness do not describe any pathogen or toxin production, but rather simple spoilage from *Bacillus subtilis* growth in dough. Such low-quality dough would not be suitable for bread production by commercial bakeries and so Envera, LLC considers this particular food exposure scenario to be unlikely and the risk to be negligible. The risk posed to adults, infants and children from food-related exposures to *Bacillus subtilis* is minimal due to the demonstrated lack of acute oral toxicity/pathogenicity associated with the microbial pesticide. Based on the submitted data, Envera, LLC concludes that there are no dietary risks that exceed the Agency's level of concern.

ii. *Drinking water.*

Because *Bacillus amyloliquefaciens* is ubiquitous in the environment, exposure to the microbe through drinking water may already be occurring and likely will continue to occur. While the proposed use sites do not include direct application to aquatic environments, the intended use of *Bacillus amyloliquefaciens* strain ENV503 is treatment of growing crops, pre- and post-harvest applications, and/or seed for the control of plant disease. If such uses were to result in pesticide spray drift or runoff that were to reach surface or ground waters, there is the potential for human exposure to *Bacillus amyloliquefaciens* residues, albeit greatly diluted, in drinking water. Municipal drinking water treatment processes and deep water wells, however, would both further reduce any such residues. More importantly, even if oral exposure to this ubiquitous microbe should occur through drinking water, due to its demonstrated lack of acute oral toxicity/ pathogenicity, Envera, LLC concludes that there is a reasonable certainty that no harm will result from such exposure.

2. *Non-dietary exposure.*

The pesticide uses of *Bacillus amyloliquefaciens* both those currently allowed and the additional proposed uses are limited to commercial agricultural and horticultural settings. There are no residential uses. Nonetheless, because *Bacillus amyloliquefaciens* is naturally occurring and ubiquitous in the environment, the potential for non-dietary, non-occupational exposure to its residues for the general population, including infants and children, is likely since populations have probably been previously exposed (and likely will continue to be exposed) to background levels of the microbe. However, neither such common human exposures to *Bacillus amyloliquefaciens* naturally present in soils, waters and plants, nor exposures associated with similar *Bacillus amyloliquefaciens* strains used internationally in producing food-grade products and fermented foods, have resulted in reports of disease or other effects. Finally, while the literature includes accounts of *Bacillus amyloliquefaciens* infections in humans (which consistently are reported only in otherwise-compromised individuals), those reports are most notable for their rare and

exceptional nature.

EPA's previous evaluation of the referenced high-dose Tier I acute toxicity and pathogenicity tests resulted in the assignment of Toxicity Category IV (least toxic), and determinations of not infective and not pathogenic, for all exposure routes. No toxicological end points of concern were identified. There are no dietary endpoints that exceed EPA's Level of Concern (LOC). Envera notes that the Agency has previously determined that any additional exposure to the microbe resulting from residues attributable to *Bacillus amyloliquefaciens* pesticide use will not result in additional aggregate non-occupational risk from dermal and inhalation exposures. This conclusion, based solely on non-occupational exposures, is consistent with EPA's determination that no occupational risks exceed the Agency's LOC, meaning that even regular occupational exposures associated with this active ingredient pose negligible risk.

E. Cumulative Effects

No mechanism of toxicity in mammals has been identified for *Bacillus amyloliquefaciens*. Therefore, no cumulative effect with other related organisms is anticipated. Because the available data demonstrate a lack of toxicity/pathogenicity potential for *Bacillus amyloliquefaciens*, adverse dietary effects are unlikely.

F. Safety Determination for U.S. population and Infants and children.

Based on the acute toxicity information discussed in section C, Envera believes that the Agency will conclude that there is a reasonable certainty that no harm will result to the United States population, including infants and children, from aggregate exposure to residues of *Bacillus amyloliquefaciens* strain ENV503. This includes all anticipated dietary exposures and all other exposures for which there is reliable information. This conclusion is based on the data available on *Bacillus amyloliquefaciens* which demonstrate a lack of toxicity/ pathogenicity potential. Thus, there are no threshold effects of concern and, as a result, Envera concludes that the additional tenfold margin of safety for infants and children is unnecessary in this instance. Further, the need to consider consumption patterns, special susceptibility, and cumulative effects does not arise when dealing with pesticides with no demonstrated significant adverse effects.

G. Effects on the Immune and Endocrine Systems

Bacillus amyloliquefaciens is a ubiquitous organism in the environment that is non-toxic to mammals. To date, there is no evidence to suggest that *Bacillus amyloliquefaciens* affects the immune system, functions in a manner similar to any known hormone, or that it acts as an endocrine disruptor. Indeed, the submitted toxicity/ pathogenicity studies in

rodents indicate that, following several routes of exposure, the immune system is intact and able to process and clear *Bacillus amyloliquefaciens*. Therefore, it is unlikely that this organism will have estrogenic or endocrine effects.

H. Existing Tolerances

There currently is no existing US exemption from the requirement of a tolerance for residues of *Bacillus amyloliquefaciens* ENV503.

I. International Tolerances

No Codex maximum residue level (MRL) exists for *Bacillus amyloliquefaciens ENV503*.

Receipt for Tolerance Petition

S: 998077 Milestone Email: james@wagnerreg.com

Regulatory Type: Tolerance Petition Resubmission: Yes No

Application Type: New Registration Fee For Service: Yes No

Billable: Yes No

Company: 87645 ENVIERA, LLC

Risk Mgr: Biologicals & Pollution Prevention Division, PM Team 91

Petition #: 7F8546 Fee Waived: Yes No Fee:

Petition Type: F - Raw Agricultural Commodity

Print Letter

Enter More Information

Tracking

Application Date: 23-Jan-2017 OPP Rec'd Date: 24-Jan-2017

Front End Date: 25-Jan-2017 Risk Manager Send Date:

FFS Due Date: Negotiated Due Date:

OPP Target Date:

Fast Track: New Ingredient:

Receipt Content: De

View/Edit

Receipt Description:

Portal submission pkg. #16873. Registration of new active ingredient, food use and Petition for Tolerance exemption.

New Ingredient Request Date

New Ingredient Received Date

Form A: Signature Date: Form B: Signature Date:

STUDY TITLE

ENV503 Biofungicide MPCA Containing *Bacillus amyloliquefaciens* strain ENV503
Petition Proposing an Exemption from the Requirement for a Tolerance

TEST GUIDELINES

N/A

AUTHOR

James M. Wagner

DATE

December 12, 2016

Submitter

Envera, LLC
220 Garfield Ave.
West Chester, PA 19380

CLAIM OF CONFIDENTIALITY

No claim of confidentiality, on any basis whatsoever, is made for any information contained in this document. I acknowledge that information not designated as within the scope of FIFRA sec. 10(d)(1)(A), (B), or (C) and which pertains to a registered or previously registered pesticide is not entitled to confidential treatment and may be released to the public, subject to the provisions regarding disclosure to multinational entities under FIFRA 10(g).

Submitter: James M Wagner **Date:** December 12, 2016

Typed Name of Signer: James M. Wagner, Agent

Typed Name of Company: Envera, LLC

GOOD LABORATORY PRACTICES COMPLIANCE STATEMENT

The information in this report is descriptive in nature and not subject to the GLP standard.

Submitter/Sponsor: James M Wagner **Date:** December 12, 2016

Typed Name of Signer: James M. Wagner, Agent

Typed Name of Company: Envera, LLC

PETITION PROPOSING AN EXEMPTION FROM THE REQUIREMENT FOR A TOLERANCE FOR THE USE OF THE MICROBIAL PEST CONTROL AGENT ***BACILLUS AMYLOLIQUEFACIENS*** STRAIN ENV503

Petition Date

December 12, 2016

Petition Author

James Wagner

Wagner Regulatory Associates

Petition Sponsor

Envera, LLC
220 Garfield Avenue
West Chester, PA 19380

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Section A - Name, Identity, and Composition of ENV503 Biofungicide containing Bacillus amyloliquefaciens strain ENV503 MPCA

Data reports supporting Section A of this petition have been submitted to EPA as part of the application to register the product "ENV503 Biofungicide MUP" which contains the microbial pest control agent (MPCA) ***Bacillus amyloliquefaciens*** strain ENV503. Citations for supporting data are included at the end of this section.

Identity of the Microbial Pest Control Agent

Name of the organism:	***Bacillus amyloliquefaciens* strain ENV503**
Taxonomy:	Kingdom: Eubacteria Phylum: Firmicutes Class: Bacilli Order: Bacillales Family: Bacillaceae Genus: Bacillus Species: amyloliquefaciens
Species, subspecies, strain:	strain ENV503
Identification / detection :	The technical grade of the active ingredient is a rod-shaped, gram positive, aerobic, motile bacterium. This MCPA is ubiquitous in nature. The technical grade of the active ingredient does not have any impurities that are on any toxic substances list. *B. amyloliquefaciens* has been reported to produce small antibiotic peptides and peptidolipids and are active against Gram-positive bacteria, but can be active against some Gram-negative bacteria, yeast, and fungi.
Culture collection:	The pure culture was isolated from *Bacillus subtilis* GB03, fermented under aeration in liquid culture medium. The culture is deposited at USDA, ARS-NCAUR, North University Street, Peoria, Illinois 61604. The culture accession number is NRRL-B-59994.
Minimum concentration of the MPCA used for manufacturing of the product ENV503 Biofungicide:	Bacillus amyloliquefaciens strain ENV503 – 5.5×10^{10} CFU/g

Bacillus amyloliquefaciens strains occur ubiquitously in nature. The primary habitat of the species is the soil and in plant litter. The isolation of various *Bacillus amyloliquefaciens* strains from soils has been reported in many regions of the world. It has also been isolated from plants including peppers, potatoes, vines and rice.

The ENV503 culture has been identified as a clean, pure isolate of *Bacillus subtilis* strain GB03. A pure culture of this strain was deposited at the United States Department of Agriculture, Agriculural Research Service, National Center for Agricultural Utilization Research. The accession number is NRRL-B-59994.

Origin and natural occurrence:	Originally isolated from an EPA registered *Bacillus subtilis* product, strain GB03. *Bacillus amyloliquefaciens* was previously classified as *Bacillus subtilis* var. *amyloliquefaciens.* Both species names are used interchangeably throughout this report.
Target organism(s):	Control and suppression of fungal and bacterial plant diseases such as Alternaria spp., Botrytis spp., Pythium and Rhizoctonia spp., and Anthracnose spp.
Mode of action:	Colonization of roots, leaves, and other plant surfaces, killing pathogenic organisms. *Bacillus amyloliquefaciens* strain ENV503 colonizes plant root hairs, leaves, and other surfaces, preventing establishment of disease-causing fungi and bacteria.
Host specificity:	The species *B. amyloliquefaciens* attacks a wide range of fungal and bacterial diseases.
Life cycle:	Spores germinate and the vegetative cells grow on the plant surface.
Infectivity, dispersal and colonization ability:	*B. subtilis* is widely distributed throughout the environment, particularly in soil, air, and decomposing plant residue. It has shown a capacity to grow over a wide range of temperatures including that of the human body (Claus and Berkeley, 1986). However, *B. subtilis* does not appear to have any specialized attachment mechanisms typically found in organisms capable of colonizing humans

(Edberg, 1991). Given its ubiquity in nature and the environmental conditions under which it is capable of surviving, *B. subtilis* could be expected to temporarily inhabit the skin and gastrointestinal tract of humans, but it is doubtful that this organism would colonize other sites in the human body (Edberg, 1991).

Relationship to known plant, animal or human pathogens:

Reviews of *Bacillus* infections from several major hospitals suggest that *B. subtilis* is an organism with low virulence. Idhe and Armstrong (1973) reported that *Bacillus* infections were encountered only twelve times over a 6-1/2 year period. Species identification of these *Bacillus* infections was not made. In another hospital study over a 6-yr. period, only two of the 24 cases of bacteremia caused by *Bacillus* (of a total of 1,038 cases) were due to *B. subtlis* (as cited by Edberg, 1991). Many of these patients were immunocompromised or had long term indwelling foreign bodies such as a Hickman catheter.

Genetic stability:

The transfer of gene sequences between strains of *B. subtilis* has been demonstrated when the strains were grown together in soil (Graham and Istock, 1979). In addition, Klier et al. (1983) demonstrated the ability of *B. subtilis* and *B. thuringiensis* to exchange high frequency transfer plasmids. Other studies have shown that *B. subtilis* has the ability to express and secrete toxins or components of the toxins that were acquired from other microorganisms through such transfers of genetic material. *B. subtilis* expressed subunits of toxins from *Bordatella pertussis* (Saris et al., 1990a, 1990b), as well as subunits of diphtheria toxin (Hemila et al., 1989) and pneumolysin A pneumococcal toxin (Taira et al., 1989). Although *B. subtilis* does not appear to possess indigenous virulence factor genes, it is theoretically possible that it may acquire such genes from other bacteria, particularly from closely related bacteria within the genus.

Information on the production of relevant metabolites (especially toxins):

A review of the literature by Edberg (1991) failed to reveal the production of toxins by *B. subtilis*. Although it has been associated with outbreaks of food poisoning (Gilbert et al., 1981 and Kramer et al., 1982 as cited by Logan, 1988), the exact nature of its involvement has not been established. *B. subtilis*, like other closely related species in the genus, *B. licheniformis, B. pumilus,* and *B. megaterium*, have been shown to be capable of producing lecithinase, an enzyme which disrupts membranes of mammalian cells. However, there has not been any correlation between lecithinase production and human disease in *B. subtilis*.

B. subtilis does produce an extracellular toxin known as amyloliquefaciensin. Although amyloliquefaciensin has very low toxigenic properties (Gill, 1982), this proteinaceous compound is capable of causing allergic reactions in individuals who are repeatedly exposed to it (Edberg, 1991). Sensitization of workers to amyloliquefaciensin may be a problem in fermentation facilities where exposure to high concentration of this compound may occur. Exposure limits to amyloliquefaciensin are regulated by Occupational Safety and Health Administration (OSHA) (29 CFR 1900, et seq.)

Resistance/sensitivity to antibiotics/anti-microbial agents used in human or veterinary medicine:

B. subtilis is not a human pathogen, nor is it toxigenic like some other members of the genus. The virulence characteristics of the microorganism are low. According to Edberg (1991) either the number of microorganisms challenging the individual must be very high or the immune status of the individual very low in order for infection with *B. subtilis* to occur.

Data Citations for Section A:

MRID 50159804: ENV503 Biofungicide MUP, *Bacillus amyloliquefaciens* strain ENV503, Product Analysis: Product Identity, Manufacturing Process, Deposition of a Sample, Discussion of Formation of Impurities, Analysis of Samples, Certification of Limits, Envera, LLC, December 2, 2016.

From: notification@pay.gov
To: James Wagner
Subject: Pay.gov Payment Confirmation: PRIA Service Fees
Date: Monday, January 23, 2017 9:56:14 AM

Your payment has been submitted to Pay.gov and the details are below. If you have any questions regarding this payment, please contact Michael Yanchulis at (703) 347-0237 or yanchulis.michael@epa.gov.

Application Name: PRIA Service Fees
Pay.gov Tracking ID: 26085L4H
Agency Tracking ID: 75170644213
Transaction Type: Sale
Transaction Date: 01/23/2017 09:56:08 AM EST

Account Holder Name: Michael Matheny

Transaction Amount: $7,575.00
Card Type: Visa
Card Number: **********4659

Registration Number:
Company Name: Envera LLC
Company Number: 87645
Action Code: B590

THIS IS AN AUTOMATED MESSAGE. PLEASE DO NOT REPLY.

Wagner Regulatory Associates, Inc.
P.O. Box 640
7217 Lancaster Pike, Suite A
Hockessin, Delaware 19707

Submitted Electronically

January 23, 2017

Document Processing Desk (REGFEE)
Attn: Kimberly Nesci, Microbial Pesticide Branch
Office of Pesticide Programs (7504P)
U.S. Environmental Protection Agency
Room S-4900, One Potomac Yard
2777 South Crystal Drive
Arlington, VA 22202-4501

Re: Application to register the products 'ENV503 Biofungicide MUP' and 'ENV503 Biofungicide Wettable Powder' containing the new active ingredient *Bacillus amyloliquefaciens strain ENV503* and Petition for Exemption from Tolerance

Dear Ms. Nesci:

Wagner Regulatory Associates, Inc., as agent for Envera LLC, is submitting the enclosed application for registration of the above referenced products containing *Bacillus amyloliquefaciens strain ENV503* together with a Petition for Exemption from Tolerance.

An application and petition were previously submitted to the Agency on December 26, 2014 for ENV503 Biofungicide MUP (*Bacillus subtillis strain ENV503*) and assigned Reg. No. 87645-E. That application was rejected on July 1, 2015 (OPP Decision Number 498696). Please note that *Bacillus amyloliquefaciens* was previously classified as *Bacillus subtilis* var. *amyloliquefaciens*[1].

This submission qualifies as "PRIA Category B590 – New active ingredient; food use; petition to establish a tolerance exemption." Envera is requesting a Small Business PRIA 75% Fee Waiver for this submission which has been submitted under separate cover.

In support of this request for ENV503 Biofungicide MUP the following documents and reports are attached:

- Letter from Envera LLC appointing Wagner Regulatory Associates, Inc. as its agent
- Application for Pesticide Registration (8570-1)
- Confidential Statement of Formula (8570-4)
- Certification with Respect to Citation of Data (8570-34)
- Data Matrix, internal and public copy (8570-35)
- Data Transmittal Document
- Supporting Data as outlined in the Data Transmittal
- Draft labeling
- A copy of the receipt confirming payment of 25% of the PRIA fee for B590 - $7,575
- Petition for Tolerance Exemption
- Notice of Filing for Tolerance Exemption

In support of this request for ENV503 Biofungicide Wettable Powder the following documents and reports are attached:

- Application for Pesticide Registration (8570-1)
- Confidential Statement of Formula (8570-4)

[1] Priest, F., Goodfellow, M., Shute, L., and Berkeley, R. 1987. "*Bacillus amyloliquefaciens* sp. nom., nom. rev." *International Journal of SystematicBacteriology*. 37: 69–71. *http://ijs.sgmjournals.org/content/37/1/69.full.pdf*.

- Formulators Exemption Statement (8570-27)
- Data Matrix, internal and public copy (8570-35)
- Supporting Data as outlined in the Data Transmittal
- Draft labeling

In the previous application for 87645-E, the Agency identified the following deficiencies which have been addressed in this current submission as follows:

Deficiency 1. The 16s RNA sequencing does not show that the ENV503/505 isolates are identical to *B. subtilis* GB03. The alignment data is not clearly represented, and it is not clear whether the alignment percentages are E values (measuring the similarity of sequences). You must demonstrate that ENV 503/505 are indeed B. subtilis GB03. Biochemical tests specified in *Bergey's Manual of Systematic Bacteriology* for *B. subtilis* must be used on ENV 503/505 and Bacillus subtilis GB03, including those tests that show variability within the species. Further, the Bacillus subtilis GB03 should be obtained from a recognized culture collection if possible.

Envera response: The requested clarification, supporting information and EPA acceptance of same following a meeting with the Agency on September 29, 2015 is included in the enclosed report "ENV03 Biofungicide MUP Bacillus amyloliquefaciens ENV503 Product Analysis: Product Identity, Manufacturing Process, Deposition of a Sample, Discussion of Formation of Impurities, Analysis of Samples, Certification of Limits".

Agency Comment. Regarding isolate identity, we (EPA) had previously requested biochemical tests to demonstrate that for those phenotypic metabolic variances within the species that the ENV503/505 isolates and *B. subtilis* GB03 act in the same manner. The biochemical tests to be performed are those listed by Bergey that identify phenotypic variations within the species.

Envera response: The requested clarification and supporting information is included in the "ENV03 Biofungicide MUP Bacillus amyloliquefaciens ENV503 Product Analysis: Product Identity, Manufacturing Process, Deposition of a Sample, Discussion of Formation of Impurities, Analysis of Samples, Certification of Limits" report submitted with this application for registration.

Agency Comment. Regarding isolate history, we cannot rely solely on your statement that you isolated *B. subtilis* GB03 from the registered product Companion. Since you indicated that the registrant of *B. subtilis* GB03 is not granting you access to their ATCC deposit, you must somehow address the isolate history in another way. Possible options may include 1) providing a chain of custody or other verification that the ENV503/505 isolates are *B. subtilis* GB03 and came from Companion, and 2) have your testing laboratory, Accugenix, isolate *B. subtilis* GB03 from Companion themselves and document this and then, add it to the reference strains they compare against in their 16sRNA analyses and then have them rerun ENV503/505 isolates against this new reference strain.

Envera response: The requested clarification and documentation is included in the "ENV03 Biofungicide MUP Bacillus amyloliquefaciens ENV503 Product Analysis: Product Identity, Manufacturing Process, Deposition of a Sample, Discussion of Formation of Impurities, Analysis of Samples, Certification of Limits" report submitted with this application for registration.

Deficiency 2. The product tested in the cited study for the acute eye irritation requirement is not similar to your product and no acute oral toxicity on the manufacturing use product was submitted or cited. You must submit data or waiver requests that take the inert composition of your manufacturing use product into account for 870.1100 Acute Oral and 870.2400 Acute Eye Irritation requirements.

Envera Response: Studies for 870.1100 Acute Oral and 870.2400 Acute Eye Irritation have been completed using ENV503 Biofungicide MUP and final reports are being submitted with this registration application.

Deficiency 3. The label states 2.5 x 10^{10} viable spores/g and that this is not consistent with the CSF. Both the label and CSF must match. You must also include the company address, EPA registration number, and net weight on the label.

Envera Response: The correct concentration for the label is 5.5 x 10^{10} spores/g to match the CSF. The label has been revised to the correct concentration and the company address, EPA registration number and net weight is added and copy enclosed with this application.

EPA Response: Screen deficiency adequately addressed.

Deficiency 4: You must modify the phrase "This product may be used for formulating end-use pesticide products..." to read "This product may be used for formulating end-use seed treatment pesticide products..." If the intent is to formulate products other than seed treatment ones, you will have to submit 885.4380 Honey Bee Testing data and resubmit waiver requests or data for freshwater and estuarine fish and invertebrate requirements.

Envera Response: It is Envera's intent to formulate products other than seed treatment products. Envera has submitted citation and discussion of data for GB03 for freshwater and estuarine fish and invertebrates and for Honey bees under MRID 49539103.

EPA Response: Screen deficiency adequately addressed provided EPA Deficiency 1 is adequately addressed.

If you need to contact me regarding this submission I can be reached at the telephone number and email address listed below. Thank you for your assistance with this application.

Sincerely,

James M. Wagner
Agent for Envera LLC
Telephone: (302) 635-7290; Email: james@wagnerreg.com

Enclosures