Steven Giardino
President and CEO
Medical Research Collaborative, LLC
7901 4th Street, North
Suite 4081
St. Petersburg, FL 33702

Re: Docket No. FDA-2019-P-3265 NOV 2 6 2019

Dear Mr. Giardino:

This letter responds to your citizen petition received on July 8, 2019, requesting that the Food and Drug Administration (FDA or the Agency) remove United States Patent No. 8,188,146 (the '146 patent) from listing in FDA's *Approved Drug Products With Therapeutic Equivalence Evaluations* (the Orange Book).[1] For the reasons described below, your petition is denied.

FDA's regulations implementing the patent listing provisions of the Federal Food, Drug, and Cosmetic Act[2] (the FD&C Act) require that an applicant submitting a new drug application (NDA); an amendment to an NDA; or, except as provided in § 314.53(d)(2) (21 CFR 314.53(d)(2)), a supplement to an approved NDA submit the patent information described in § 314.53(c) to its NDA on declaration Forms FDA 3542a and 3542 with the filing or upon and after approval, respectively.[3] The information requested in Form FDA 3542 must be provided for any patent that claims the approved drug substance, approved drug product, or any approved method of using the drug and with respect to which a claim of patent infringement could reasonably be asserted if a person not licensed by the patent owner engaged in the manufacture, use, or sale of the drug.[4]

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[1] The '146 patent was submitted for listing in the Orange Book as both a drug substance (patent code "DS") and drug product (patent code "DP") patent on June 26, 2017, in connection with Amarin Pharmaceuticals Ireland Limited's NDA 202057 for Vascepa (icosapent ethyl) capsules. Vascepa was approved by FDA on July 26, 2012, and is currently marketed in the United States as 0.5-gram (0.5-g) and 1.0-g capsules. We note that your citizen petition does not indicate whether your request to delist the '146 patent is being made in connection with the 0.5-g strength, the 1.0-g strength, or both strengths.

[2] Sections 505(b)(1) and (c)(2) of the FD&C Act (21 U.S.C. 355(b)(1) and (c)(2)).

[3] See § 314.53(b).

[4] See § 314.53(b) and § 314.53(c)(2)(ii); see also section 505(b)(1) of the FD&C Act.

FDA publishes certain information from Form FDA 3542 in the Orange Book after approval of the NDA or the supplement.[5] For example, all patent numbers with their corresponding expiration dates are listed for each approved drug product.[6] Drug substance and drug product patents are indicated as such with the symbols "DS" or "DP," respectively, in the patent codes column of the Orange Book. Method-of-use patents are indicated with the symbol "U" followed by a number, known as a "use code," representing a brief description of the patented method of use provided by the NDA holder.[7] FDA plays a ministerial role in the publication of the patent information, including use codes, submitted by an NDA holder in the Orange Book. In other words, FDA does not review the patent(s) identified by an NDA holder in Form FDA 3542 to evaluate the appropriateness of the NDA holder's patent listing(s) or the accuracy of its use code(s).[8]

FDA has established a process, described in its regulations at § 314.53(f), by which any person can dispute the accuracy or relevance of a patent listing.[9] Generally, § 314.53(f)(1) provides that a person disputing the accuracy or relevance of patent information submitted to FDA and published in the Orange Book, or claiming that such information is incomplete, must first notify the Agency in writing, setting forth a statement of dispute that describes the specific grounds for disagreement. The notification must be titled "314.53(f) Patent Listing Dispute" and must be directed to the Orange Book Staff.[10] For disputes concerning patent information regarding a

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[5] See § 314.53(e); see also sections 505(b)(1), (c)(2), and (j)(7) of the FD&C Act.

[6] In connection with NDA 202057, the Orange Book lists January 27, 2020, as the expiration date of the '146 patent.

[7] See § 314.53(c)(2)(ii)(P)(3).

[8] See "Applications for FDA Approval to Market a New Drug: Patent Submission and Listing Requirements and Application of 30-Month Stays on Approval of Abbreviated New Drug Applications Certifying That a Patent Claiming a Drug Is Invalid or Will Not Be Infringed; Final Rule" (68 FR 36676 at 36687 (June 18, 2003)) (2003 Final Rule) ("We note that we will not evaluate a patent to assess whether the declaration is accurate or whether the patent has been appropriately submitted for listing . . . We will, however, review the declaration for completeness and to determine that the information given by the NDA applicant or holder or patent owner indicates that the patent is eligible for listing"). We note that the Medicare Prescription Drug, Improvement, and Modernization Act of 2003 (MMA) (Public Law 108-173) superseded certain provisions of the 2003 Final Rule related to 30-month stays of approval; the superseded regulations were subsequently revoked by technical amendment. See 69 FR 11309 (March 10, 2004).

[9] Notwithstanding that FDA does not review patents, the Agency has taken various steps to ensure that patents submitted to NDAs for listing in the Orange Book meet the criteria set out in sections 505(b)(1) and (c)(2) of the FD&C Act. For example, the 2003 Final Rule included new regulations at § 314.53 describing specifically what types of patents must and must not be submitted to FDA. More recently, the Agency revised its regulations at § 314.53 to clarify and improve the procedures that govern challenges to the accuracy or relevance of the NDA holder's submission of patent information to the Agency. See, generally, "Abbreviated New Drug Applications and 505(b)(2) Applications; Final Rule" (81 FR 69580 (October 6, 2016)).

[10] Specifically, "[t]he patent listing dispute communication should be directed to the Central Document Room, Attn: Orange Book Staff, Center for Drug Evaluation and Research, Food and Drug Administration, 5901-B Ammendale Rd., Beltsville, MD 20705-1266, or to the Orange Book Staff at the email address listed on the Agency's Web site at http://www.fda.gov" (§ 314.53(f)(1)).

drug substance or drug product claim, the Agency will send an unredacted copy of the statement of dispute to the applicable NDA holder and request that the holder "confirm the correctness of the patent information . . . or withdraw or amend the patent information . . . within 30 days of the date on which the Agency sends the statement of dispute."[11] FDA will not change patent information in the Orange Book unless the NDA holder withdraws or amends its patent information.[12]

Because your request disputes the appropriateness of listing the '146 patent and urges FDA to remove it from the Orange Book, your request is subject to the procedures and requirements set forth in our regulations at § 314.53(f). Submission of your request to FDA in a citizen petition does not comply with those procedures, and we are unable to resolve your concerns in a citizen petition response. Therefore, your citizen petition is denied without comment on the merits of the petition's statements regarding the '146 patent.[13]

Sincerely,

Janet Woodcock, M.D.
Director
Center for Drug Evaluation and Research

[11] See § 314.53(f)(1)(i)(A).

[12] Id.

[13] Notwithstanding the denial of your citizen petition, our regulations permit you to submit a patent listing dispute to the Orange Book Staff that accords with the procedures and requirements set forth at § 314.53(f).