FDA U.S. FOOD & DRUG ADMINISTRATION

May 3, 2019

By Certified Mail – Return Receipt Requested

[redacted]

Re: Citizen Petition for Due Diligence Determination of Patent Term Extension for Absorb GT1 Bioresorbable Vascular Scaffold (BVS) System; Docket Nos. FDA-2017-E-3592 and FDA-2017-E-3616

Dear [redacted]:

This letter responds to your due diligence petition (hereafter Petition), dated January 31, 2019. Your Petition requests that the Food and Drug Administration (FDA or the Agency) determine that Abbott Vascular, Inc. (Abbott or the applicant), the applicant for a patent term extension for the Absorb GT1 Bioresorbable Vascular Scaffold (BVS) System (Absorb GT1) device, is not entitled to any of the requested period of patent term extension because Abbott did not act with due diligence during the regulatory review period.

As the Chief Scientist, I am authorized to perform all delegable functions of the Commissioner of Food and Drugs.[1] I have reviewed your Petition and the attached exhibits, Abbott's response to the Petition, and the applicable statutory provisions and regulations. For the reasons set forth below, I find that the Petition fails to contain information or allegations upon which it may reasonably be determined that Abbott did not act with due diligence during the regulatory review period. In addition, it also appears from the record before me that the Petition was not filed in accordance with 21 CFR 60.30(d).

I. Background

A. Absorb GT1

Absorb GT1 is "indicated for improving coronary luminal diameter in patients with ischemic heart disease due to de novo native coronary artery lesions ≥2.5 mm to ≤3.75 mm in diameter in lesions."[2]

On December 12, 2012, Abbott's investigational device exemption (IDE) under section 520(g) of the Federal Food, Drug, and Cosmetic Act (FDCA) for Absorb GT1 became effective.[3] On July 1, 2015, Abbott submitted a premarket approval application (PMA) for Absorb GT1, and FDA approved it on July 5, 2016.[4]

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[1] FDA Staff Manual Guide 1410.21 ¶ 1.B.7.
[2] 83 Fed. Reg. 65680, 65681 (December 21, 2018).
[3] *Id.*
[4] *Id.*

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B. Drug Price Competition and Patent Term Restoration Act of 1984

The Drug Price Competition and Patent Term Restoration Act of 1984 (Public Law 98-417) and the Generic Animal Drug and Patent Term Restoration Act (Public Law 100-670) generally provide that a patent may be extended for a period of up to five years so long as the permission for commercial marketing is the first permitted commercial marketing or use of the product and the patented item (medical device, human drug product, animal drug product, food additive, or color additive) was subject to regulatory review by FDA before the item was marketed. Under 35 U.S.C. 156(c), a product's regulatory review period forms the basis for determining the amount of extension an applicant may receive.

A regulatory review period is the sum of two periods of time: a testing phase and an approval phase. For medical devices for which an IDE is required, the testing phase begins on the effective date of the IDE and ends on the date that an applicant initially submits a PMA.[5] The approval phase, as relevant to this matter, begins on the initial submission date for the PMA and ends upon approval.[6] The United States Patent and Trademark Office (USPTO) applies several statutory limitations in its calculations of the actual period for patent term extension. Among other limitations, the maximum length of a patent term extension is calculated based upon the sum of the length of the approval phase and one-half the length of the testing phase.[7] A maximum of five years can be added to a patent term.[8] In all cases, the total patent life for the product with the patent term extension cannot exceed fourteen years from the product's approval date. If the patent life of the product after approval has fourteen or more years, the product would not be eligible for patent term extension.[9]

C. Absorb GT1 Patent Term Extension History

Abbott submitted a patent term restoration application to the USPTO for Absorb GT1 (U.S. Patent Nos. 7,971,333 and 8,323,329).[10] In response to the USPTO's request for FDA's assistance in determining the patent's eligibility for patent term restoration, FDA informed the USPTO that Absorb GT1 had undergone a regulatory review period and that the approval represented the first permitted commercial marketing or use of the product.[11] In response to the USPTO's request that FDA determine the product's regulatory review period, on December 21, 2018, FDA published a Federal Register notice setting forth the dates on which it based its determination and determined that the regulatory review period for Absorb GT1 is 1,303 days.[12] FDA found that, of this time, 932 days occurred during the testing phase of the regulatory review period, while 371 days occurred during the approval phase. FDA's Federal Register notice established the deadline for submitting a due diligence petition as June 19, 2019.[13]

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[5] *See* 35 U.S.C. 156(g)(3)(B)(i); 21 CFR 60.22(c)(1)(i).
[6] *See* 35 U.S.C. 156(g)(3)(B)(ii); 21 CFR 60.22(c)(2)(i).
[7] 35 U.S.C. 156(c)(2).
[8] 35 U.S.C. 156(g)(6).
[9] 35 U.S.C. 156(c)(3).
[10] 83 Fed. Reg. 65680, 65681 (December 21, 2018).
[11] *Id.*
[12] *Id.*
[13] *Id.*

II. Discussion

A. Legal Requirements for a Due Diligence Petition

A person may file with FDA a due diligence petition claiming that an applicant for patent term extension did not act with due diligence in seeking FDA approval of the product during some part of the regulatory review period. FDA regulations establish the filing, formatting, and content requirements for due diligence petitions. Among other requirements, due diligence petitions must include sufficient facts to merit an investigation by FDA of whether the applicant acted with due diligence during the regulatory review period and a certification that the petitioner provided a true and complete copy of the petition to the applicant by certified or registered mail (return receipt requested) or by personal delivery.[14] If the petition fails to comply with these requirements, FDA may deny the petition.[15] FDA may also deny the petition without further investigation if the "petition fails to contain information or allegations upon which it may reasonably be determined that the applicant did not act with due diligence during the applicable regulatory review period."[16]

The due diligence standard is "that degree of attention, continuous directed effort, and timeliness as may reasonably be expected from, and are ordinarily exercised by, a person during a regulatory review period."[17] FDA examines the facts and circumstances of the applicant's actions during the regulatory review period to determine whether the applicant acted with due diligence.[18] FDA will consider all relevant factors, such as the amount of time between the approval of an investigational exemption and the commencement of a clinical investigation and the amount of time required to conduct a clinical investigation.[19]

The preambles to the proposed and final rules for 21 CFR part 60 help to further illuminate FDA's approach to due diligence petitions.[20] In those preambles, FDA relied extensively on principles in the legislative history in explaining the intent of the regulations.[21] As noted in the legislative history itself, due diligence petitions are not intended to cause a review of every action, but to identify significant periods when the loss of patent term resulted "solely from the applicant's failure to pursue approval."[22]

B. Analysis

1. Claims of Alleged Failure to Act with Due Diligence

In your Petition, you assert that Abbott did not act with due diligence during the regulatory review period for four reasons.

First, you state that that Abbott "failed to exhibit an adequate degree of attention to fundamental human factors and usability engineering principles."[23] You claim that Abbott's product design caused a change

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[14] 21 CFR 60.30(c)-(d).
[15] 21 CFR 60.34(b)(1), (b)(4).
[16] 21 CFR 60.34(b)(4).
[17] 35 U.S.C. 156(d)(3); 21 CFR 60.36(a).
[18] 21 CFR 60.36(a).
[19] *Id.*
[20] 51 Fed. Reg. 25338 (July 11, 1986); 53 Fed. Reg. 7298 (Mar. 7, 1988).
[21] 51 Fed. Reg at 25342-43; 53 Fed. Reg. at 7304.
[22] H. Rept. 857, 98th Cong., 2d Sess. Part 1 at 42 (June 21, 1984).
[23] Petition at 4.

in implantation technique and that, because of that change, Abbott should have assessed the need for mandatory training early in the design and development process as part of its design verification and validation.[24] You claim that Abbott was aware that Absorb GT1 was "less deliverable" than XIENCE[25] and that Absorb GT1 "came with a learning curve."[26] You conclude that, based on your decades of experience with medical devices, Abbott's "unlawful domestic marketing of the unapproved [Absorb GT1] despite actual knowledge that new users found the device more difficult to impact shows a lack of the due diligence as may reasonably be expected from . . . companies that produce significant risk devices."[27]

Next, you claim that Abbott "engaged in prohibited anti-competitive conduct."[28] You allege that Abbott engaged in "monopoly leveraging" and used illegal marketing tactics, such as off-label promotion of the XIENCE product family, to "supplant its own metallic stent market share by introducing its new, more profitable [Absorb GT1] products."[29] You also state that Abbott engaged in "supracompetitive pricing" and that, in the international market, Absorb GT1 was sold for two to three times the price of traditional metallic drug-eluting stents.[30]

Third, you assert that Abbott "failed to exhibit continuous direct effort to protect the rights, safety, and welfare of human subjects of research."[31] You claim that Abbott promoted the unapproved Absorb GT1 product family to physicians in the United States.[32] You present a summary of alleged illegal promotional activities Abbott engaged in before FDA approved the IDE for Absorb GT1 and a summary of alleged illegal promotional activities Abbott engaged in after receiving IDE approval but before FDA approved the PMA.[33] You allege that Abbott's PMA for Absorb GT1 was untimely because Abbott engaged in a domestic marketing campaign "years before the IDE was approved."[34] Further, you state that Abbott's promotion of Absorb GT1 in the United States before IDE approval was an "illegal incitement of unregulated human medical experimentation."[35] Additionally, you allege that Abbott illegally marketed Absorb GT1 outside of the United States for an "unauthorized clinical treatment."[36]

Lastly, you state that Abbott "failed to comply with regulatory requirements despite credible evidence of non-compliance."[37] In support of your assertion, you reference Abbott's "persistent attempts" to have 21 CFR 812.7 rescinded, a FDA warning letter from FDA in 2007, and an investigation into Abbott's practices by the United States Senate.[38] In further support of your allegation, you also describe your tenure at Abbott, including the circumstances of your departure, as well as procedural history relating to a separate matter involving Abbott.[39]

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[24] *See id.*
[25] You do not include any information about XIENCE, but based on an internal search, XIENCE is part of a family of FDA-approved eluting coronary stents. The PMAs for these devices are held by Abbott.
[26] *See* Petition at 4.
[27] *See id.* at 4-5.
[28] *Id.* at 5.
[29] *See id.*
[30] *See id.*
[31] *Id.*
[32] *See id.*
[33] *See id.* at 6-7.
[34] *Id.* at 8.
[35] *See id.*
[36] *See id.*
[37] *Id.* at 9.
[38] *See id.*
[39] *See id.* at 9-10.

You argue that Abbott's "misconduct" posed a preventable threat to public health. You conclude that, for the reasons described above, FDA should determine that Abbott did not act with due diligence during the regulatory review period and deny Abbott's patent term extension request "in its entirety."[40]

As explained above, the due diligence standard is "that degree of attention, continuous directed effort, and timeliness as may reasonably be expected from, and are ordinarily exercised by, a person during a regulatory review period."[41] Due diligence petitions are not intended to cause a review of every action, but to identify significant periods when the loss of patent term resulted "solely from the applicant's failure to pursue approval."[42]

Even assuming the truth of your allegations, none of the allegations describes actions that (1) relate to the appropriate factors for evaluating regulatory review period or (2) identify significant periods when the loss of patent term resulted from Abbott's failure to pursue approval of its PMA. Your allegations relating to Absorb GT1's design do not establish that Abbott failed to pursue approval of its PMA. Your allegations suggest merely that you disagree with the steps taken by Abbott during the course of device development. Even if the new design necessitated additional training before use, that additional requirement is not relevant to whether Abbott acted with due diligence during the regulatory review period. Likewise, your allegations about Abbott's pricing and promotional activities have no connection to the regulatory review period for Absorb GT1. The Petition does not link how domestic or international pricing or promotional schemes lengthened the regulatory review period or kept Abbott from pursuing approval of its PMA. Specifically, your summaries of promotional activity seem to mostly describe scientific presentations at medial conferences. Regarding the alleged marketing that occurred before the IDE was approved, you fail to link how that marketing affected the length of the regulatory review period or how it caused Abbott to fail to pursue approval of its PMA with proper due diligence. Lastly, the allegations relating to your departure from Abbottas well as your allegation relating to Abbott's "misconduct" do not relate to the regulatory review period and fail to demonstrate how Abbott failed to pursue approval of its PMA.[43]

A due diligence petition must include sufficient facts to merit an investigation by FDA of whether the applicant acted with due diligence during the regulatory review period.[44] If the petition fails to contain information or allegations upon which it may reasonably be determined that the applicant did not act with due diligence during the regulatory review period, FDA may deny the petition without considering the merits.[45] For the reasons explained above, I have determined that the Petition fails to contain information and allegations upon which it may reasonably be determined that Abbott did not act with due diligence during the regulatory review period.

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[40] *See id.* at 10-11.
[41] 35 U.S.C. 156(d)(3); 21 CFR 60.36(a).
[42] *See* H. Rept. 857, 98th Cong., 2d Sess. Part 1 at 42 (June 21, 1984).
[43] Similarly, to the extent your Petition makes arguments relating to Absorb GT1's trade name and Abbott's "umbrella marketing" of its Bioresorbable Vascular Scaffold (BVS) brands, these arguments have no clear bearing on Abbott's diligence during the regulatory review period for Absorb GT1. *See* Petition at 2-3.
[44] 21 CFR 60.30(c).
[45] 21 CFR 60.34(b)(4).

2. Certification

Although, as discussed above, sufficient grounds exist to deny the petition based on 21 C.F.R. 60.34(b)(4), the record before me also suggests that you may have failed to comply with the regulatory requirements for filing a Petition as set forth in 21 CFR 60.30.

Your Petition contains a statement that the Petition had been served on Abbott "by certified US mail (return receipt requested)" at Mark Lupkowski, "Attorney of Record."[46] In Abbott's response to your Petition, Abbott states that you did not send Abbott the Petition; rather, you sent the petition to Abbott's counsel.[47] Additionally, Abbott contends that counsel received the Petition only by United States Postal Service Priority Mail Express, not by registered or certified mail, and has submitted a mailing label in support of this position.[48]

The regulations for due diligence petitions at 21 CFR 60.30(d) require that the petition contain a certification that the petitioner has served a true and complete copy of the petition upon the applicant by certified or registered mail (return receipt requested) or by personal delivery. FDA may deny a due diligence petition without considering the merits if the petition is not filed in accordance with 21 CFR 60.30.[49]

The regulations are unambiguous: a petitioner must certify that it has served the petition on the applicant by certified or registered mail (return receipt requested) or personal delivery, and the regulations do not provide for service by any other means. While your petition contains a certification that you served a true and complete copy of the petition upon the applicant by certified mail (return receipt requested), Abbott has provided credible evidence that you did not serve the company in the required manner. Therefore, it appears that you failed to serve Abbott in the required manner and that thus 21 CFR 60.34(b)(1) would provide an alternative ground for the Agency to deny the Petition.

III. Conclusion

For the foregoing reasons, I find that the Petition fails to contain information or allegations upon which it may reasonably be determined that Abbott did not act with due diligence during the regulatory review period. It also appears that you did not file the in accordance with 21 CFR 60.30(d). Therefore, I am denying your Petition.

Sincerely,

RADM Denise Hinton
Chief Scientist

cc: Michael K. Stern, Counsel for Abbott, Covington and Burling LLP

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[46] Petition at 13.

[47] *See* Petition Response at 9.

[48] *See id.* at 9; *see also* Petition Response Exhibit 1.

[49] 21 CFR 60.34(b)(1).