January 31, 2019

Dockets Management Staff (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852

RE: Docket Nos. FDA-2017-E-3592 and FDA-2017-E-3616

CITIZEN PETITION

The undersigned ("Petitioner") submits this petition under 21 CFR 60.30(a) of the Federal Food, Drug, and Cosmetic Act to request the Commissioner of Food and Drugs to initiate an investigation by FDA of whether the Applicant for patent extension for the Absorb GT1 Bioresorbable Vascular Scaffold (BVS) System acted with due diligence during the regulatory review period. See Docket Nos. FDA-2017-E-3592 and FDA-2017-E-3616.

All supplemental materials accompanying this submission are part of the unredacted citizen petition and this information must be treated as confidential. The unredacted citizen petition cannot be entered into the public docket because some of the information is sealed by court order. Petitioner is a former employee of the Applicant, where she worked in Medical Affairs as a field manager in a medical science liaison role for the Northeastern United States. Her job title was "Regional Medical Science Manager-Northeast." Her geographic territory included the District of Columbia and the following states: Connecticut, Maine, Massachusetts, New Hampshire, Rhode Island, Vermont, New Jersey, New York, Pennsylvania, Delaware, Virginia, Maryland, and West Virginia. She was hired in mid-2010 and she was terminated on May 9, 2014. Petitioner currently has a lawsuit pending in the Federal District Court for the District of Massachusetts for wrongful

termination in violation of public policy and False Claims Act retaliation. This citizen petition is based on the same conduct described in her civil case. See Case # 1:14-cv-13155-IT.

I. ACTION REQUESTED

Petitioner requests an FDA investigation and a final determination that the Applicant did not act with due diligence during the Absorb GT1 Bioresorbable Vascular Scaffold (BVS) System regulatory review period.

II. STATEMENT OF GROUNDS

Petitioner alleges that the Applicant did not act with due diligence during the regulatory review period and shall set forth sufficient facts, including dates, to that effect. The FDA's publication of the regulatory review period determination under sec. 60.20 found in this docket uses a misnomer for the product for which the patent extension is sought. The Applicant refers to the product by the tradename, "Absorb GT1 Bioresorbable Vascular Scaffold (BVS) System." In contrast, when describing PMA Number P150023, FDA categorizes the product's "Generic Name" as "Absorbable Coronary Drug-Eluting Stent." The correct product tradename is a material fact in this due diligence determination because product naming conventions are a known source of medical error and iatrogenic injury. Specifically, an instructive coronary stent incident occurred in 2009 where product naming confusion induced medical errors that posed a threat to patient safety.

In September 2009, Boston Scientific issued a field correction stating that they received reports from cardiac cath labs that TAXUS Liberte Drug Eluting coronary stents had been inadvertently selected when the physician intended to implant a Liberte Bare-Metal stent, and Liberte Bare-Metal stents had been inadvertently selected when the physician intended to implant a TAXUS Liberte Drug-Eluting stent. Because of the importance in accurate device selection to patient safety, the company renamed the bare-metal device "VeriFLEX" and FDA classified the action as a Class II Recall. The Liberte recall is instructive for understanding how a company's marketing practices, such as leveraging the brand recognition of a product family name, can be in direct conflict with protecting patient safety and thwarting preventable medical errors.

Petitioner alleges that the Applicant engaged in widespread, worldwide illegal marketing of the company's "Bioresorbable Vascular Scaffold" (BVS) brands, where the monikers "Bioresorbable Vascular Scaffold" and "BVS" are tradenames that the Applicant selected and then marketed to brand the company's product family. That product family includes at least three (3) extensions: "ABSORB," "ABSORB GT1" and "ESPRIT." These three names are brand extensions of the Bioresorbable Vascular Scaffold (BVS) brand family. This marketing practice is sometimes called "umbrella branding." Umbrella branding is not *per se* illegal, however, the timing of the Applicant's BVS marketing practices constitutes prohibited conduct because the Applicant's BVS marketing campaign was initiated and executed long before the mandatory pre-market approval authorization was granted by FDA on July 5, 2016.

Petitioner alleges that the Applicant willfully violated the following regulations:

21 CFR 50
21 CFR 56
21 CFR 812
21 CFR 814

A final determination that the Applicant did not act with due diligence during the Absorb GT1 Bioresorbable Vascular Scaffold (BVS) System regulatory review period is warranted for these reasons:

A. Applicant failed to exhibit an adequate degree of attention to fundamental human factors and usability engineering principles,
B. Applicant engaged in prohibited anti-competitive conduct,
C. Applicant failed to exhibit continuous directed effort to protect the rights, safety, and welfare of human subjects of research,
D. Applicant failed to comply with regulatory requirements despite credible evidence of non-compliance.

Petitioner provides a detailed explanation and supporting evidence for each of these allegations within this in the paragraphs that follow.

A. Applicant failed to exhibit an adequate degree of attention to fundamental human factors and usability engineering principles

The Boston Scientific LIBERTE stent recall is instructive about potential perils of product name choice. But the public health risk due to potential product name confusion when the Applicant's product brand name is disguised as a generic description is further exacerbated by the fact that safe and effective BVS implantation requires a change in physician technique compared to the products it replaces. The Applicant's own product design decision, specifically regarding strut dimensions, caused the need for a change in implantation technique.

It is a well-established design principle in human factors and usability engineering "that the systems of which humans are a part call forth errors from humans, not the other way around." [1] In 2010, the Applicant instructed the Petitioner in her onboarding training materials[2] that strut thickness is a known contributor to thrombosis events. This design decision should have prompted an assessment of the need for mandatory training early in the design and development process as part of design verification and validation. The Applicant was aware of the risks associated with increasing strut dimensions by 2010.

As of 2013, the Applicant was also aware that BVS was less deliverable than XIENCE and that using the BVS device came with a learning curve. Petitioner created two (2) self-recorded audio files[3] in October 2013 in preparation for exhibit booth duty at the Transcatheter Cardiovascular Therapeutics (TCT) meeting, where she and her colleagues were expecting to address medical information requests from clinicians. The two recordings summarize the most frequently asked questions received about BVS as of October 2013 based on Petitioner's conversations with other company employees. The Applicant's decision to pursue unlawful domestic marketing of the unapproved BVS product despite actual knowledge that new users found the device more difficult to implant shows a lack of the due diligence as may reasonably be expected from, and is ordinarily

[1] Moray, N. (1994). "Error Reduction as a Systems Problem." Human Error in Medicine, Marilyn Sue Bogner (Ed)., Hillsdale, NJ: Lawrence Erlbaum Associates, Inc.

[2] See folder titled "Onboarding Training Materials" containing scanned training binders that Petitioner received from the applicant after she was hired

[3] Petitioner prepared a list of frequently asked questions in preparation for exhibit booth duty at TCT 2013. She created the self-recordings titled "WS_10105" and "WS_10106" on the same day in October 2013 to prepare for that event. Each audio file and its transcript is included with this petition. Petitioner can also provide the original recording device, a handheld digital recorder, to FDA upon request. See folder "Self-Recordings and Transcripts."

exercised by companies that produce significant risk medical devices. Petitioner bases the preceding statement on her two decades of experience with the research, design, development, and commercialization of medical devices used in cardiovascular, neurological, and other clinical applications.

B. Applicant engaged in prohibited anti-competitive conduct

Until the contract expiration, about 7 of every 10 stents was manufactured by the Applicant because the Applicant had an agreement[4] with Boston Scientific to manufacture the PROMUS stent as a private-label version of XIENCE. Executing a marketing campaign for the only absorbable drug-eluting stent during this period allowed the company to use monopoly power in one market to realize a competitive advantage in a second market. This tactic is a species "monopoly leveraging." Petitioner alleges the Applicant was holding market share by using illegal marketing tactics, including off-label promotion of its XIENCE product family, as part of a cannibalization strategy. In other words, the Applicant intended to supplant its own metallic stent market share by introducing its new, more profitable BVS products. Petitioner also alleges that the Applicant engaged in supracompetitive pricing. The Applicant was exercising market power internationally since BVS was being sold for two to three times the price[5] of traditional metallic drug-eluting stents. Here, Applicant's supracompetitive pricing is evidence that its anti-competitive behavior had driven competition out of the market.

C. Applicant failed to exhibit continuous directed effort to protect the rights, safety, and welfare of human subjects of research

Applicant promoted the unapproved BVS product family to physicians in the United States without premarket approval (PMA) in violation of the Federal Food Drug and Cosmetic Act, which contains a comprehensive regulatory scheme prohibiting the conduct described in this petition.

[4] http://news.bostonscientific.com/news-releases?item=59079
[5] https://www.mddionline.com/abbotts-bioresorbable-stent-successful-asia-market-absorbs-higher-prices

Specifically see:

21 CFR 50
21 CFR 56
21 CFR 812
21 CFR 814

A summary of illegal promotional activities executed by the Applicant in the United States before the IDE was granted on 12/12/2012 is provided in the following table:

Domestic PROMOTIONAL ACTIVITIES executed by the Applicant BEFORE THE IDE WAS GRANTED ON 12/12/2012		
DATE	TITLE	COMMENT
08/2010	Will Bioresorbable Vascular Scaffolding Replace Drug Eluting Stents?	Applicant supported this TCT event with an "educational grant"
12/2010	DES in the SFA: Will it ever work?	Applicant's employee presentation posted at CRTOnline.org
11/2011	Bioabsorbable Stent Platforms: The Vision and New Questions in Eastern and Western Patients	Applicant's employee presentation at TCT
11/2011	Development Of Bioresorbable Scaffold Platforms For The Peripheral Vasculature: Can The Excellent Coronary Results Of The ABSORB TRIAL With Everolimus Polylactide Be Duplicated In Peripheral Arteries	Applicant's employee presentation at VEITHsymposium
10/2012	Development of a Bioresorbable Scaffold for the SFA	Applicant's employee presentation at TCT
11/2012	Long-term results of the ABSORB trial showing benefits of biodegradable coronary stents: when will we know if they will work elsewhere	Applicant's employee presentation at VEITHsymposium

Note: "TCT" is the Transcatheter Cardiovascular Therapeutics (TCT) meeting that was held in the United States and organized by Cardiovascular Research Foundation (CRF). VEITHsymposium is a meeting that was held in the United States and Continuing Medical Education (CME) was provided through The Cleveland Clinic Foundation Center for Continuing Education. The Applicant supported these meetings with funding.

A summary of illegal promotional activities executed by the Applicant in the United States after the IDE was granted on 12/12/2012, but before the PMA was granted on 07/05/2016, is provided in the following table:

Domestic PROMOTIONAL ACTIVITIES executed by the Applicant after 12/12/2012, but BEFORE THE PMA WAS GRANTED ON 07/05/2016		
DATE	TITLE	COMMENT
02/2013	Update on the Development of BVS: Challenges for the Development of Polymeric Biodegradable Scaffolds for Peripheral Vascular Intervention	Applicant's employee presentation at CRT
03/2013	Interview describing the "bioresorbable scaffold future as the next— what we're calling the 'Fourth Revolution of Coronary Angioplasty.' "	Applicant's employee interview posted at http://www.cardiotube.net/?p=2755
10/2013	Bioresorbable Vascular Scaffolds: The Next Greatest Thing	Applicant's employee presentation at VIVA
03/2014	Recent Clinical Data for Metallic Drug-Eluting Stents (DES) and Bare Metal Stents (BMS) from Major Meta-Analysis Studies	Applicant disseminated this promotional newsletter without adequate labeling (internal routing number SE2939496 Rev. B 03/14)
07/2014	BioResorbable Vascular Scaffolds: Transformational Technology for PCI	3-day course organized by CRF with lecture by Applicant's employee
07/2014	Recent Clinical Data for Durable and Bioresorbable polymer Drug- Eluting Stents (DES) and Bare Metal Stents (BMS) from Major Meta- Analyses Studies	Applicant disseminated this promotional newsletter to physicians without adequate labeling (internal routing number SE2940007 Rev. A 07/14)
09/2014	Absorb Fully Bioresorbable Vascular Scaffold (BVS): Emerging Real- World Clinical Data and Optimal Implant Techniques	Applicant disseminated this promotional newsletter to physicians without adequate labeling (internal routing number SE2940254 Rev. A 09/14)
10/2014	Update on Absorb from TCT 2014	Applicant disseminated this promotional newsletter to physicians without adequate labeling (internal routing number SE2940457 Rev. A 10/14)
10/2014	Major DAPT Randomized Trial Results at AHA and the CoCr-EES Subgroup Results	Applicant disseminated this promotional newsletter to physicians without adequate labeling (internal routing number SE2940659 Rev. A)
11/2014	Update on Supera	Applicant disseminated this promotional newsletter to physicians without adequate labeling (internal routing number SE2940556 Rev. A 11/14)
05/2015	Drug-Eluting Bioabsorbable Stents: Is This the Future of SFA and Popliteal Disease	Applicant's employee presentation at New Cardiovascular Horizons (NCVH) Conference focusing on Peripheral Artery Disease
07/2015	Bioresorbable Vascular Scaffold: The Fourth Revolution in Interventional Cardiology	Keynote lecture title for the Geoffrey O. Hartzler, MD Interventional Cardiology Symposium Program held at The Sheraton Maui, Resort & Spa

Note: CRT is the Cardiovascular Research Technologies meeting held in the United States and organized by Medstar Washington Hospital Center. VIVA is the Vascular InterVentional Advances ("VIVA Physicians") meeting held in the United States. Applicant supported these meetings with funding.

Petitioner alleges that the Applicant's 2015 PMA submission was untimely because the Applicant was already engaged in a domestic marketing campaign by 2010, years before the IDE was approved in 2012. This conduct exposed the public to unnecessary and entirely preventable risks associated with unauthorized implantation. Petitioner alleges that the BVS Device Master Record (DMR) contains hazards for which labeling is the purported risk mitigation, but that no FDA-approved labeling existed before July 2016. Consequently, the BVS marketing and promotional materials that were disseminated in the United States before July 2016 were not accompanied by adequate labeling. Furthermore, BVS marketing and promotional materials were disseminated in the United States before December 2012, when BVS was an *experimental*, not an investigational, medical implant. Therefore, the BVS promotion was illegal incitement of unregulated human medical experimentation.

Petitioner also alleges that the Applicant illegally marketed Absorb BVS to physicians in Australia in December 2014 at VERVE Symposium as an unauthorized clinical treatment for peripheral vascular disease below the knee. The applicant did not exhibit timeliness in seeking an IDE for peripheral investigation of Absorb BVS as a treatment for peripheral vascular disease below the knee. The IDE study for Absorb BVS (NCT01751906) use in coronary arteries included clinical trial sites in the United States and Australia. The Absorb BVS device was being sold commercially in Australia as of 2013 according to the Australian Register of Therapeutic Goods (ARTG). There are two (2) clinical trials identifiers associated with BVS for treating peripheral vascular disease below the knee. The first study is NCT01341340, a clinical trial that was terminated in 2012. The second study, NCT02793349, was not initiated until 2015. Consequently, Petitioner alleges that there was no IDE for BVS use for peripheral vascular disease below the knee when the illegal marketing for that application occurred at VERVE in December 2014. Petitioner alleges that the BVS Device Master Record (DMR) does not contain labeling for BVS where the indications include peripheral vascular disease below the knee. Therefore, none of the BVS devices shipped after 12/2014 from the United States manufacturing facility to Australia (i.e. introduced interstate commerce) contained adequate labeling for the illegally promoted BVS clinical use as a treatment for peripheral vascular disease below the knee. BVS was subject to a Class I recall in 2017. The

BVS registration mark in Australia[6] was eventually withdrawn and Petitioner alleges this action was taken to protect patients from unauthorized implantation that could be induced by the Applicant's willful misconduct.

D. Applicant failed to comply with regulatory requirements despite credible evidence of non-compliance

The Applicant clearly understood the requirements under 21 CFR 812.7 as is illustrated by the company's persistent attempts to have to have that regulation rescinded in 2002.[7] In addition the Applicant received an FDA Warning letter issued in 2007 regarding very similar misconduct. In 2010, the year Petitioner was hired, the Applicant was embroiled in a United States Senate Committee on Finance investigation of the company's practices with respect to cardiac stent usage at St. Joseph's Medical Center in Maryland.

Petitioner sought advice from her supervisors in 2013 regarding inappropriate attempts by an Applicant executive to influence the scientific findings of a physician researcher. When the situation continued to deteriorate, she initiated compliance report 1402ABT10003 [8] in February 2014, a report that she continually supplemented with more information as the situation escalated. She was granted leave under FMLA beginning 03/24/2014. On 04/13/2014, she took a computer screen shot of this illegal directive from her supervisors based on goals and objectives for 2014: "Increase Absorb's penetration into the PCI market." While on that leave, on April 30th, she asked to be placed on paid leave. Her leave request was not granted and instead she was fired on May 9, 2014. Petitioner received a paper check[9] for wages from the applicant dated 5/16/2014 in violation of the Massachusetts Wage Act. She was not paid in full for wages on the date of her discharge, an action that is inconsistent with the Applicant's own policy[10] and a violation of state law. Her termination notice also indicates that she was fired before the corporate compliance investigation she initiated was completed.

[6] See folder "BVS in Australia"
[7] See folder "Public comments from Applicant"
[8] See folder "Compliance Report 1402ABT10003"
[9] See "check stub image.jpg"
[10] See folder "Corporate Policies"

Concerned by the clinical implications of the GHOST-EU study results announced in July 2014, Petitioner promptly filed a qui tam complaint under seal three (3) weeks later. She alleges illegal promotional newsletters were being disseminated in the same timeframe as the seal period. The Applicant modified the company Code of Conduct at the beginning of 2015, after her complaint was unsealed, but Petitioner offers evidence herein of another illegal marketing incident at the Hartzler Symposium in Maui within months of that revision. In parallel, the Applicant sought and obtained a Motion to Dismiss the Petitioner's entire civil lawsuit in April 2016, while implying that her action was founded on only two presentations: "Relator alleges Abbott gave two presentations concerning ABSORB that purportedly violated FDA regulations prohibiting the promotion of "investigational" medical devices."[11] Petitioner timely appealed and the operative first amended complaint, alleging ongoing misconduct throughout the regulatory review period, was docketed on 07/08/2016, just three days after FDA granted BVS pre-market approval. Despite actual knowledge of these illegal promotional events and the Petitioner's persistent effort to report the wrongful conduct internally in the first instance, the Applicant filed a Motion to Dismiss her wrongful termination in violation of public policy claim in May 2017. The Applicant's motion was denied. The docket allowing Petitioner to challenge the Applicant's patent extension was opened in December 2018. Even in the face of repeated reports, warnings, and complaints, the Applicant continually chose financial and competitive advantage over patient safety during the entire regulatory review period.

III. CONCLUSION

The Applicant's misconduct posed a known, but entirely preventable threat to the public health and the misconduct occurred repeatedly both before and during the regulatory review period. Despite a litany of investigations, a senate report, an FDA warning letter, and multiple complaints filed in federal court, Applicant failed to correct egregious misconduct. Therefore, Petitioner alleges that the Applicant willfully misrepresented the number of days in the regulatory review period wherein the Applicant did not act with due diligence as "0 days" on page 19 of the September 2016 patent extension application.

[11] See "Memo of law in support of defendant's motion to dismiss for failure to state a claim" at docket entry 15 in case # 1:14-cv-13155-IT

The regulations at 21 CFR 60.36(b) plainly state:

> *"For purposes of this part, the actions of the marketing applicant shall be imputed to the applicant for patent term restoration. The actions of an agent, attorney, contractor, employee, licensee, or predecessor in interest of the marketing applicant or applicant for patent term restoration shall be imputed to the applicant for patent term restoration."*

Petitioner has provided sufficient information to support her allegation that the Applicant engaged in illegal marketing and commercialization practices in violation of the Federal Food, Drug and Cosmetic Act during the entire regulatory review period, posing a preventable danger to the public. The United States Supreme Court says that "the decision to grant a patent is a matter involving public rights—specifically, the grant of a public franchise."[12] Applicant's repeated willful misconduct to the public's detriment warrants enforcement action, not further extension of a public franchise award. For these reasons, a final determination that the Applicant did not act with due diligence during the regulatory review period is warranted and Applicant's patent extension request for the Absorb GT1 Bioresorbable Vascular Scaffold (BVS) System should be denied in its entirety.

IV. OTHER REQUIRED INFORMATION

A. Environmental Impact

The action requested in this petition is subject to categorical exclusion under 25.30, 25.31, 25.32, 25.33, or 25.34 of this chapter or an environmental assessment under 25.40 of this chapter.

B. Economic Impact

Pursuant to 21 C.F.R. § 10.30, an economic impact statement will be submitted upon request of the Commissioner following review of the petition.

[12] See slip op. *Oil States Energy Services, LLC v. Greene's Energy Group, LLC*, 584 U.S. ___ (2018)

C. Certification

The undersigned certifies on _____, that, to the best knowledge and belief of the undersigned, this petition includes all information and views on which the petition relies, and that it includes representative data and information known to the Petitioner which are unfavorable to the petition.

_____(Signature)

Ebonia Elliott-Lewis, Petitioner

35 Draper Ave

Westwood, MA 02090

781-769-3905

JURAT

Commonwealth of Massachusetts

County of Norfolk

On this _____ day of _____, 20_____, before me, the undersigned notary public, personally appeared ___Ebonia Elliott-Lewis___ ("Petitioner"), proved to me through satisfactory evidence of identification, which were United States passport and Massachusetts driver's license, to be the person who signed the preceding document in my presence, and who swore or affirmed to me that the contents of the document are truthful and accurate to the best knowledge and belief of the Petitioner.

_____(Signature)

Notary Public

D. Certificate of Service on the Applicant for patent extension

The undersigned certifies, that Petitioner served a true and complete copy of the petition upon the Applicant by certified US mail (return receipt requested) on _____ to this address:

Mark Lupkowski
Registration No. 49,010
Attorney of Record
275 Battery Street Suite 2600
San Francisco, CA 94111

_____(Signature)

Ebonia Elliott-Lewis, Petitioner

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