DEPARTMENT OF HEALTH AND HUMAN SERVICES

FOOD AND DRUG ADMINISTRATION

CENTER FOR DEVICES AND RADIOLOGICAL HEALTH

PROCEEDING ON THE PROPOSAL TO DISQUALIFY

DR. MICHAEL A. ARATA

FROM RECEIVING INVESTIGATIONAL TEST ARTICLES

COMMISSIONER'S DECISION

In this proceeding under 21 CFR part 16, the Food and Drug Administration's (FDA's or the Agency's) Center for Devices and Radiological Health (CDRH), pursuant to 21 CFR part 812, proposed that Dr. Michael A. Arata (Dr. Arata) be disqualified from receiving test articles under 21 CFR part 812 and be ineligible to conduct any clinical investigation that supports an application for a research or marketing permit for products regulated by FDA. CDRH has moved to deny Dr. Arata's request for a hearing under 21 CFR 16.26(a) and to disqualify him under 21 CFR 812.119. As the Acting Chief Scientist, I have the authority to perform all delegable functions of the Commissioner of Food and Drugs (Commissioner).[1]

Based upon my review of the parties' submissions, I find that there is no genuine and substantial issue of fact with regard to whether Dr. Arata repeatedly violated 21 CFR part 812. I am therefore granting CDRH's motion to deny Dr. Arata's request for a hearing. Pursuant to 21 CFR 812.119(b), I am issuing this Commissioner's Decision disqualifying Dr. Arata from eligibility to receive test articles under 21 CFR part 812 or to conduct any clinical investigation that supports an application for a research or marketing permit for products regulated by FDA.

[1] FDA SMG 1410.21 "General Redelegations of Authority from the Commissioner to Other Officers of the Food and Drug Administration" at ¶ 1.B.7; ¶ 1.D.

I. Background

Dr. Arata is President of Synergy Health Concepts, Inc. (Synergy Health), a medical clinic in Newport Beach, California. FDA conducted an inspection of Synergy Health from April 10 through May 15, 2012, which resulted in FDA's issuing Dr. Arata a Warning Letter, dated September 5, 2012. FDA cited multiple violations of FDA's regulations in 21 CFR parts 812 and 50. On September 24, 2012, Dr. Arata responded to the Warning Letter. FDA conducted another inspection of Synergy Health between November 16, 2015, and January 28, 2016. During this inspection, FDA found that Dr. Arata was continuing to commit many of the same violations that were addressed in the Warning Letter.

On September 13, 2016, CDRH sent Dr. Arata a Notice of Initiation of Disqualification Proceedings and Opportunity to Explain (NIDPOE), which outlined the basis for CDRH's conclusion that Dr. Arata has repeatedly and deliberately violated 21 CFR parts 812 and 50. The NIDPOE explained the basis for each violation and offered Dr. Arata an opportunity to respond in writing or at an informal conference. Dr. Arata requested an informal conference, and it occurred on October 25, 2016. At the informal conference, Dr. Arata provided a slide presentation and verbal explanations responding to the NIDPOE. After reviewing all the available information, including the information Dr. Arata provided at the informal conference, CDRH concluded that Dr. Arata failed to adequately address the violations set forth in the NIDPOE.

On June 21, 2017, the Associate Commissioner for Regulatory Affairs issued Dr. Arata a Notice of Opportunity for Hearing (NOOH) asserting repeated or deliberate violations of 21 CFR part 812 and 50. The violations alleged in the NOOH are:

1. Repeated failure to submit an application to the FDA and obtain IRB and FDA approval prior to allowing subjects to participate in an investigation, in violation of 21 CFR 812.20, 812.40, and 812.42;
2. Deliberate allowance of subjects to participate in a study before obtaining approval from the reviewing IRB prior to initiation of the study, in violation of 21 CFR 812.100 and 812.110(a);
3. Deliberate failure to ensure that IRB-approved informed consent was obtained from study subjects and adhere to informed consent requirements, in violation of 21 CFR 50.20, 50.25(a)(1), 50.27(a), and 812.100;
4. Deliberate representation of a device as safe and as effective for the purpose of treating various diseases other than those for which FDA has approved them, in violation of 21 CFR 812.7(d); and
5. Repeated failure to maintain accurate and complete records of receipt, use, and disposition of devices, in violation of 21 CFR 812.140(a)(2).

The NOOH provided Dr. Arata an opportunity to request a hearing under 21 CFR part 16. The NOOH explained that hearings are granted only if there is a genuine and substantial issue of fact and that a hearing will not be granted on issues of policy or law.

On July 14, 2017, Dr. Arata requested a hearing. On September 17, 2017, CDRH submitted a Motion to Deny a Hearing and to Disqualify and a memorandum in support of that Motion. CDRH recommends that Dr. Arata's request for a hearing be denied because the material Dr. Arata submitted raises no genuine and substantial issue of fact and that the Commissioner disqualify Dr. Arata. This memorandum includes multiple exhibits, which I reference throughout this decision.

II. Analysis

Under 21 CFR 812.119, a clinical investigator will be disqualified from eligibility to receive test articles and to conduct certain clinical investigations if the Commissioner determines, after evaluating all available information, that the investigator has repeatedly or deliberately failed to comply with the requirements of 21 CFR part 812, 50, or 56. A showing that the clinical investigator "repeatedly" or "deliberately" violated the relevant FDA regulations is sufficient to disqualify an investigator under 21 CFR 812.119.

The Commissioner may deny a request for a hearing, in whole or in part, under 21 CFR 16.26(a), if the Commissioner, or the delegate who has authority to make the final decision on the matter, finds that the materials submitted do not raise a genuine and substantial issue of fact. The standard for denial of a hearing in 21 CFR 16.26(a) aligns with the standard in federal court for summary judgment. *See Hess & Clark, Div. of Rhodia, Inc. v. Food & Drug Admin.*, 495 F.2d 975, 983 (1974) (While discussing an FDA order withdrawing approval of a new animal drug application, the court stated, "When the FDA issues a Notice of Opportunity for Hearing, its summary judgment procedures are available if the requesting party fails to raise material issues of fact."). A material factual dispute is one that would affect the outcome of the proceeding.

Dr. Arata's primary argument in support of his request for a hearing is that he did not conduct clinical investigations and therefore did not violate any of the regulations cited in the NOOH. In support of this position, Dr. Arata argues that he was only practicing medicine and sharing information from his medical practice. He also argues that he never intended to conduct a clinical investigation. Evaluating Dr. Arata's arguments, I find that he raises no genuine and substantial issue of fact concerning whether his conduct constituted an investigation of the Bard device, as "investigation" is defined by FDA's regulations. Indeed, the undisputed record before me establishes that Dr. Arata repeatedly failed to obtain an approved investigational device exemption (IDE) and approval by an institutional review board (IRB) before conducting investigations requiring such approvals under FDA's regulations. Accordingly, I find that Dr. Arata repeatedly violated 21 CFR 812.20, 812.40, and 812.42.

During the informal conference with CDRH, Dr. Arata conceded that, if the conduct described in the three articles referenced in the NOOH is appropriately understood to constitute clinical investigations, then his conduct would be governed by the requirements in 21 CFR part

812.[2] Indeed, the crux of whether Dr. Arata is entitled to a hearing in this proceeding turns on whether there is a genuine and substantial issue of fact with respect to whether Dr. Arata engaged, on multiple occasions, in an "investigation" under 21 CFR 812.3(h), which "means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device."[3]

Before conducting an investigation, or part of an investigation, involving a significant risk device that has not received premarket approval or clearance for the proposed use, FDA regulations in part 812 require FDA and IRB approval.[4] The responsibilities for obtaining such approvals fall to the sponsor of the study or, as in this case, the sponsor-investigator, which is defined as "an individual who both initiates and actually conducts, alone or with others, [the] investigation." Under 21 CFR 812.20(a), a sponsor-investigator must "submit an application to FDA if [he] intends to use a significant risk device in an investigation" and "shall not begin an investigation for which FDA's approval of an application is required until FDA has approved the application." Among other requirements described in 21 CFR 812.40, a sponsor-investigator is responsible for "ensuring that IRB review and approval are obtained" and for "submitting an IDE application to FDA." Under 21 CFR 812.42, a "sponsor shall not begin an investigation or part of an investigation until an IRB and FDA have both approved the application or supplemental application relating to the investigation or part of an investigation." Considered together, these regulations require that a sponsor-investigator apply for and obtain FDA and IRB approval

[2] Memorandum in Support of CDRH's Motion to Deny a Hearing and to Disqualify Michael A. Arata, M.D. (Memorandum), Exhibit 9, Page 38, Lines 13-16.
[3] A "subject" means "a human who participates in an investigation, either as an individual on whom or whose specimen an investigational device is used or as a control. A subject may be in normal health or may have a medical condition or disease." 21 CFR 812.3(p).
[4] *See* 21 CFR 812.1 (defining the scope of 21 CFR part 812 to include investigation of devices for uses that would otherwise require premarket authorization); 812.20 (defining the circumstances of when submission of an IDE application is necessary); 812.30 (explaining how IDE applications are approved).

before conducting an investigation involving a significant risk device; therefore, conducting an investigation without obtaining such approvals on multiple occasions constitutes a repeated violation of the requirements under part 812 within the meaning of 21 CFR 812.119.

CDRH alleges that Dr. Arata, as a sponsor-investigator, repeatedly began an investigation or part of an investigation by initiating research on subjects using a significant risk device, the Bard Atlas Percutaneous Transluminal Angioplasty Balloon Dilation catheter (Bard Device), without first obtaining an approved IDE or IRB approval. A device is considered significant risk if, among other factors, it presents a potential for serious risk to the health, safety, or welfare of a subject.[5] Before addressing the current violations, CDRH references the 2012 Warning Letter, in which CDRH informed Dr. Arata that he had failed to meet his obligation regarding a clinical investigation titled, "Radiographic and Intravascular (IVUS) Evaluation of Venous Morphology During CCSVI Treatment (the IVUS study)." In the IVUS study, Dr. Arata used the Bard Device to dilate the veins in the neck and chest of multiple sclerosis (MS) subjects to treat a condition called Chronic Cerebrospinal Venous Insufficiency (CCSVI).[6] The Bard device was a cleared device but not for venous angioplasties or valvuloplasty.[7] According to the IVUS study protocol, the clinical investigation aimed to "evaluate venous morphology pre- and post-percutaneous angioplasty using an intravascular ultrasound imaging methodology" and "validate

[5] 21 CFR 812.2(m). FDA guidance explains that the risk determination is based on the proposed use of the device in an investigation and not on the device alone. "Information Sheet Guidance for IRBs, Clinical Investigators, and Sponsors; Significant Risk and Nonsignificant Risk Medical Device Studies," at 5-6 (Jan. 2006). Information relevant to the determination includes the description of the device, reports of prior investigations conducted with the device, the proposed investigational plan, and subject selection criteria. *Id.* The determination also should consider whether the subject will need to undergo an additional procedure as part of the investigational study and the potential harm the procedure may cause as well as the potential harm caused by the device. *Id.* We agree with CDRH's uncontested allegation that the Bard Device, when used to perform the CCSVI procedure and TVAM treatment, presents a potential for serious risk to the health, safety, or welfare of a subject, and therefore is a significant risk device.

[6] *See* Memorandum Exhibit 5.

[7] *See* Memorandum Exhibits 5 and 9.

the safety of valvuloplasty in various neurodegenerative disorders (such as multiple sclerosis)."[8] In the Warning Letter, CDRH explained to Dr. Arata his legal responsibilities as a sponsor-investigator, including that he must submit an IDE application for a significant risk device and that he should not begin investigations without first obtaining FDA and IRB approval.

CDRH alleges that, despite receiving the Warning Letter, Dr. Arata further studied the use of the Bard device as part of the Transvascular Autonomic Modulation (TVAM) investigation without first obtaining either IRB or FDA approval. CDRH states that the TVAM treatment is the same as the CCSVI procedure and that, as with the CCSVI procedure, Dr. Arata used the Bard device for unapproved uses in the TVAM treatment. CDRH identifies three published articles co-authored by Dr. Arata that discuss the CCSVI procedure and TVAM treatment.

The first article that CDRH references is a 2013 article co-authored by Dr. Arata and published in *Phlebology*, titled "Blood Pressure Normalization Post-jugular Venous Balloon Angioplasty." The article discusses the results of the CCSVI clinical investigation using the Bard Device that was the subject of the Warning Letter. The article states, under the methods section, that "[t]he study involved MS patients who visited [Synergy Health] between 2011 and 2012" and describes, among other things, the screening criteria used for selecting participants.[9] The article states that the study method "has been shown to have an acceptable safety profile and clinical efficacy."[10] The article further includes a note that "[the authors] are engaged in additional studies, aiming to show the close association between CCSVI and ANS dysfunction."[11]

[8] Memorandum Exhibits 1(a) and 1(c).
[9] Memorandum Exhibit 2.
[10] *Id*.
[11] *Id*.

In 2014, another article co-authored by Dr. Arata published in the *Journal of Endovascular Therapies*, titled "Transvascular Autonomic Modulation: A Modified Balloon Angioplasty Technique for the Treatment of Autonomic Dysfunction in Multiple Sclerosis Patients" (Endovascular Therapies article). The published article included the heading "Clinical Investigation" and a "METHODS" section in which he describes the screening criteria he used for subjects of the clinical investigation and the "control group" in the study.[12] The stated purpose of the clinical investigation was, "To describe the use of transvascular autonomic modulation (TVAM) to improve cardiovascular autonomic nervous system (ANS) dysfunction in multiple sclerosis (MS) patients, comparing *the safety and efficacy* of this modified technique with balloon angioplasty."[13] The article describes the clinical investigation as a "pilot study," states that "we studied the clinical safety of TVAM and its efficacy in improving ANS dysfunction," and "report[s] that TVAM does not result in an increased risk as evidenced by the absence of significant adverse events."[14] The article concludes that "[t]he safety and efficacy of TVAM in MS patients observed in this pilot study is encouraging and that "[f]urther studies should investigate TVAM in a larger MS cohort."[15]

In 2015, Dr. Arata co-authored a third article, which was published in *Hormone Metabolism Research*, titled "Neuroendocrine Responses to Transvascular Autonomic Modulation: A Modified Balloon Angioplasty in Multiple Sclerosis Patients." This article again discusses Dr. Arata's clinical "study" of MS subjects who visited Synergy Health and describes

[12] *See* Memorandum Exhibit 3.
[13] *Id* (emphasis added).
[14] *Id*.
[15] *Id*.

Dr. Arata's data from these patients as "the first study measuring endocrine response to venous dilation in MS patients."[16]

In his hearing request, Dr. Arata does not generally deny that the conduct described in these articles or the NOOH occurred, but he argues that such conduct does not constitute an investigation or series of investigations under 21 CFR 812.3(h). Insofar as he does challenge specific aspects of the conduct described in the articles and the NOOH, his challenges do not raise material disputes of fact with respect to whether he repeatedly engaged in investigations involving a significant risk device without obtaining the necessary approval by FDA or an IRB.

In support of his legal argument, Dr. Arata contends that the NOOH merely cites "isolated" aspects of his articles to demonstrate that he conducted investigations, but the factual allegations in the NOOH focus on the key considerations for CDRH's proposed finding that the conduct at issue constituted investigations of a device for a use that had never received premarket approval or clearance.

As explained above, an investigation, as defined by 21 CFR 812.3(h), involves research on one or more human subjects to determine the safety or effectiveness of a device. Dr. Arata does not contest that his use of the Bard Device for the CCSVI procedure or the TVAM treatment was beyond the scope of the cleared indications for that device or that, when employed for such uses, the Bard Device is a significant risk device. He does not contest that his procedures employed subject screening criteria. Most importantly, Dr. Arata does not dispute that the conduct at issue involved the use of the Bard Device on human subjects under research protocols employing the Bard device for use in the CCSVI procedure and TVAM treatment.

[16] Memorandum Exhibit 4.

Dr. Arata also argues that he did not use control groups when he was using the Bard Device to perform the CCSVI procedure or provide the TVAM treatment. However, a control group need not be employed for use of a device on human subjects to be an investigation under 21 CFR 812.3(h), which hinges only on whether the conduct was a clinical investigation or research to determine the safety or effectiveness of a device on human subjects.

Dr. Arata further argues that he was only engaged in the practice of medicine and sharing information in the fashion that other physicians frequently do. He also maintains that he did not intend to report the results of his research to FDA to support a Premarket Approval Application or 510(k) notification related to the Bard Device. He contends that he only intended to report "unusual results from a medical procedure that may be researched further" and that he never intended to conduct investigations regulated under part 812. Whether Dr. Arata believed he was engaged in the practice of medicine and merely reporting his observations or whether he intended to submit this data to FDA is not relevant to the definition of an investigation under 21 CFR 812.3(h). The key question is whether the research conducted by Dr. Arata was intended to determine the safety or effectiveness of a device. By describing his efforts to determine the safety and effectiveness of the Bard device for use in the TVAM treatment and CCSVI procedure, the articles co-authored by Dr. Arata conclusively demonstrate that he engaged in multiple investigations or parts of investigations.

Because I have found that there is no genuine and substantial issue of fact as to whether Dr. Arata began investigations, as defined by 21 CFR 812.3(h), it follows that is no material factual dispute with respect to whether Dr. Arata repeatedly violated the legal requirements found in 21 CFR 812.20, 812.40, and 812.42 as alleged in CDRH's first NOOH violation. As described earlier, 21 CFR 812.20 requires that a sponsor-investigator submit an IDE application

to FDA if the sponsor intends to use a significant risk device in an investigation and prohibits a sponsor from beginning an investigation until FDA approves the IDE. Here, Dr. Arata does not contest that the Bard device is a significant risk device. As explained above, Dr. Arata repeatedly engaged in investigations using the Bard device despite not applying for or obtaining an approved IDE. Under 21 CFR 812.40, sponsor-investigators are responsible for, among other things, submitting an IDE application to FDA. Dr. Arata did not submit an IDE application to FDA for his investigations relating to the CCSVI and TVAM treatment; therefore, he also violated this regulation on more than one occasion. Lastly, 21 CFR 812.42 states that a sponsor-investigator shall not begin an investigation or part of an investigation until an IRB and FDA have both approved the sponsor's application. By beginning the investigations relating to the CCSVI procedure and TVAM treatment without the required IRB and FDA approval, Dr. Arata violated 21 CFR 812.42 repeatedly.[17] In sum, Dr. Arata conducted investigations for which 21 CFR part 812 required him to obtain prior FDA and IRB approval, and he repeatedly failed to do so. Because I have found that Dr. Arata repeatedly committed the first violation described by CDRH in the NOOH by repeatedly violating his obligations under 21 CFR 812.20, 812.40, and 812.42, there is no need to address the other charges listed in the NOOH.

III. Conclusion

Based on all the information available to FDA, under 21 CFR 16.26, I find that there is no genuine and substantial issue of fact regarding whether Dr. Arata repeatedly violated the FDA's regulatory requirements in 21 CFR part 812. Therefore, I am granting CDRH's motion to

[17] In his request for hearing, Dr. Arata states that he received IRB approval for "VBDT-01 Medical Record Review Protocol" to extract data from his patient's records. He also states that the IRB waived the need for informed consent from the patients for using their information since no patient information would accompany the data. While Dr. Arata may have received IRB approval for his post-procedure data review, such approval does not address his failure to obtain IRB approval prior to beginning the CCSVI procedure and TVAM treatment research, in violation of 21 CFR 812.42.

deny Dr. Arata's request for a hearing. Moreover, pursuant to 21 CFR 812.119, I am disqualifying Dr. Arata from eligibility to receive test articles under 21 CFR part 812 and to conduct any clinical investigation that supports an application for a research or marketing permit for FDA-regulated products, including drugs, biologics, devices, new animal drugs, foods, including dietary supplements, that bear a nutrient content claim or a health claim, infant formulas, food and color additives, and tobacco products. Dr. Arata may seek to have his eligibility reinstated pursuant to 21 CFR 812.119.

___/s/__Denise M. Hinton____

RADM Denise M. Hinton

Acting Chief Scientist

Dated: May 23, 2018