DuVal Client Alert

Passing on Tribal Knowledge of FDA Law

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UNBROKEN:

The Howard Root & Vascular Solutions Acquittal

An Off-label Case About an On-label Use

INTRODUCTION/EXECUTIVE SUMMMARY

The Howard Root Story. This is a story of a CEO and a company in which the government brought a criminal case based upon the alleged off-label promotion of a 510(k) cleared medical device. Howard Root and Vascular Solutions settled a related whistleblower civil case without admission of liability by paying $520,000 to the federal government. Not satisfied with the civil settlement, the Department of Justice and U.S. Attorney's Office pursued Mr. Root and the company on criminal charges of selling an adulterated and misbranded medical device and conspiracy to do the same. Howard's legal team vigorously defended by maintaining the use was on-label and that even if it wasn't their client had the 1st Amendment right to provide truthful information about that use. The jury brought in a unanimous verdict acquitting both the CEO and company.

The device in question is the Vari-Lase Short Kit used for the treatment of varicose veins. It was cleared with a broad intended use statement for use in ablating varicose veins and for the incompetence and reflux of superficial veins in the lower extremity. The Short Kit version was promoted for use in short vein segments, which includes perforator veins. The question was whether the claims and conduct of the sales reps in promoting for use in perforator veins constituted off-label promotion in violation of the Food, Drug & Cosmetic Act.

The other story is the Louis Zamperini story. It is unfair to analogize Louis' story (in book and movie form) to the Howard Root story because Louis was a decorated World War II prisoner of war in Japanese prison camps where he was horribly tortured both physically and mentally. He was eventually freed when American forces defeated and occupied Japan. But for Howard Root there are at least some loose but compelling analogies to Louis' story.

Here are some of the general observations and takeaways we make below.

First, the government had a continuing focus on "conduct" versus speech. The government has long taken the position that it when it brings these cases it is not prosecuting speech *per se*, but using the speech as evidence of a manufacturer's intent in a prosecution for misbranding. The government has also maintained it can prosecute conduct underlying the adulteration and misbranding charges, but not the truthful off-label speech itself. The interesting thing about this theory is that none of the "conduct" really becomes actionable until there is speech/communication made to the world outside the company to effectuate the conduct. Judge Lamberth (the judge in this case) once opined, in the famous *Washington Legal Foundation* (WLF) case that the regulation of marketing and promotional activities is regulation of "conduct" only "to the extent that moving one's lips is 'conduct,' or to the extent that affixing a stamp and distributing information through the mails is 'conduct.'" *Washington Legal Foundation v. Friedman*, 13 F. Supp. 2d at 59 (D.D.C. 1998). But the Court never had to make a decision on the conduct vs speech issue because the jury unanimously acquitted the defendants.

Second, the jury instructions recognize off-label promotion for the first time. In the jury instructions, the government actually acquiesced to an unbelievable (for the government) jury instruction which, to paraphrase, stated that it is not a crime for a company or its representatives to provide wholly truthful and non-misleading information about the unapproved use of a device. This is the government arguably allowing a path for lawful off-label promotion.

Finally, it is time for FDA to rethink how it interprets general vs specific use and when new 510(k)s are required for new indications. The fact Vascular sought to "clarify" this use with FDA by proactively filing a 510(k),

does not change the analysis of whether the law required a 510(k) submission for this use. The bottom line is that the original clearance clearly encompassed this use and Vascular should not have had to submit a 510(k) to obtain it. But that is the dilemma in which industry finds itself. Industry often believes the use of its product is on-label and comfortably within the cleared general intended use statement, but is not sure whether FDA will agree or not. As such, they can market the product and face the prospect of a possible FDA warning letter or go to FDA and ask for an additional clearance knowing FDA will most likely either 1) agree it is a new indication and require a lot of data for clearance (and suggest a Pre-Submission meeting), or 2) state it is a new intended use altogether and require a de novo or PMA submission, again with a lot of data. This is the same parsing of words FDA uses today in 510(k) labeling negotiations. ***FDA is fond of clearing devices that purport to be used for everything, but can be promoted for nothing.***

Author's note: *We do not and have not ever represented Howard Root or Vascular Solutions. All Rights Reserved by Universal Studios Hollywood, for pictures of the "Unbroken" movie.*

THE ANALOGY TO THE "UNBROKEN" STORY

Louis Zamperini was a talented and promising track athlete who competed in the 1936 Berlin Olympics with Adolph Hitler present. He enlisted in the United States Army Air Forces as a Lieutenant. He served as a bombardier in B-24 Liberators in the Pacific. On a search and rescue mission, mechanical difficulties forced Zamperini's plane to crash in the ocean. Only three of the 11 crew members survived. They floated in a life raft in the ocean for 47 days. Two men survived that ordeal on the ocean and were relieved to float near the Marshall Islands, but deflated when they were captured by the Japanese Navy occupying that territory. He was taken to a series of two island prison camps, ending up in a camp in Japan where he was tortured and tormented by a prison guard, Mutsuhiro "Bird" Watanabe. The Bird

was later included in General Douglas MacArthur's list of the forty most wanted war criminals in Japan.

The loose similarities in stories. Louis was a talented track athlete with a bright future. Howard was a talented and successful corporate lawyer turned entrepreneur who started a successful medical device company. Louis' plane went down and he survived 47 days in a life raft only to be picked up by the Japanese Navy and imprisoned. Howard and his company were investigated and prosecuted for almost five years by the DOJ and U.S. Attorneys in San Antonio. Louis had the misfortune of having the "Bird" at the second and third prison camps that tormented and tortured him mercilessly. The Criminal Division demanded a guilty plea and exclusion for Mr. Root without ever having met with him. Howard had the U.S. Attorneys out of the San Antonio office and Department of Justice torment his company and his employees with threats to their livelihoods and families ending with a criminal indictment and trial. The Japanese used other prisoners to snitch on each other with promises of favorable treatment. Howard had the government make similar offers using threats of prosecution and promises of immunity to his unwitting employees to get them to turn state's evidence.

The ending. In the end, Louis' spirit was unbroken by his tormentors and he survived to be a celebrated war hero and lived a happy life as a Christian evangelist with a strong belief in forgiveness. Howard's spirit remained unbroken as well. He has become an industry hero for his courage in standing up to his tormentors at great personal risk to prove a couple of important points—that the government often has a strong and arrogant misbelief that its interpretations of the law are correct and that the government plays too fast and loose with its enormous prosecutorial power.

SOME FACTS ABOUT THE HOWARD ROOT/VASCULAR SOLUTIONS CASE

This case is about the Vari-Lase device cleared for treating varicose veins which was launched in June 2007. The facts will always be disputed by the government, but here they are depicted in a relatively straight forward fashion. The device had a general intended use statement for the following (emphasis added in bold, italics and underlining):

> "The VARI-LASE Bright Tip kit (and Console) is indicated for the treatment of ***varicose veins and varicosities associated with the Great Saphenous Vein, and*** for the treatment of ***incompetence and reflux of superficial veins in the lower extremity."***

Vascular unsuccessfully sought FDA clearance to specifically add the "perforator vein" to the labeling even though it was already impliedly encompassed by the general intended use statement. The reviewer, who was new to FDA, demanded clinical work when it wasn't required for a competitor so the 510(k) submission was withdrawn. The company's "Short Kit"— a shorter version of the Vari-Lase procedure kit to be used in treating "short vein segments" was launched in 2007 and sold for seven years totaling $532,000 in U.S. sales (less than 1/10th of 1% of company sales). Of the $58MM in sales commissions paid to company sales representatives during that period, only $40,000 in total commissions was paid for the Short Kit. There were no allegations of patient injury in using the product.

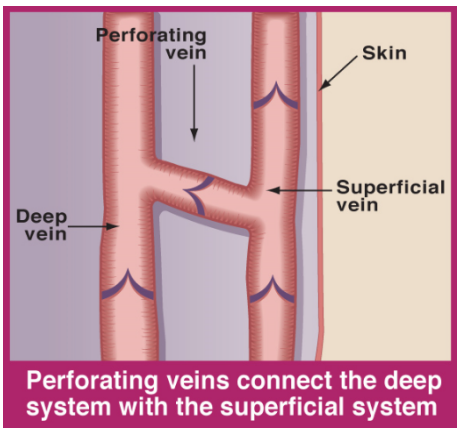
The defense offered no witnesses. The case is too long and complicated to tell the whole story so we will only attempt to distill it here. Suffice it to say the government had plenty of documents from email, PowerPoint presentations, text messages, reimbursement documents, etc. to suggest the company's sales representatives had done something nefarious and illegally promoted off-label for perforator veins. What the government didn't have, or understand, was the context for all of these communications,

i.e. plausible explanations for all of them. Nor did the government have the benefit of the fact that the defense would successfully fight the case arguing that the use in question was on-label, not off-label. The defense successfully fought this case using FDA's own guidance documents and cross-examining the prosecution's own witnesses. The company never called even one witness -- it never had to -- because the government's witnesses actually proved the company's theory. When the government rested its case, so did the defense.

Vascular demonstrated the use was on-label. The government focused on Vascular's unsuccessful effort to gain marketing authorization, without really understanding why or whether it was actually needed –- which was only under the FDA's non-binding guidance. It also focused on allegations that the sales campaign provided misleading information about the clinical trial results for the device and the availability of reimbursement for use in the perforator vein, without ever proving that these statements were false. So the case turned on whether the government could prove the use in question was off-label. But the government's case was, frankly, rather presumptive about that fact, and the judge and jury would have to take their word for it that the use was off-label. The government didn't even seem to really question the underpinnings of its position, instead focusing heavily on the "conduct" in which the company was involved. Again the government rather arrogantly assumed the jury would believe them that it was an off-label use and the company's conduct was in criminal support of marketing and selling the device for that off-label use.

Conversely, Vascular focused on the fact that the use was not off-label, but was on-label and, if that position was proven correct, the government had no case. Well, the company picked the right trial strategy. The jury believed the use to be on-label so the entire premise for the government's "off-label" case went away.

The case turned upon an analysis of an FDA guidance document entitled "General/Specific Intended Use" (General/Specific Use Guidance). If you look at the intended use statement shown above it covers a lot of territory anatomically speaking. The perforator vein, that FDA believed to be an off-label use, was deemed on-label by the jury who relied on the testimony of three key government witnesses: a physician, a highly-respected and longstanding FDA Branch Chief named Neil Ogden, and a former company employee who worked in regulatory and clinical affairs. All three witnesses, when cross-examined, believed the use to be on-label under FDA's guidance; but the most damning testimony of course came from FDA's own Neil Ogden who under cross-examination from defense counsel had to admit that the use the government believed was off-label, i.e. perforator veins could be viewed to be on-label. Here is just one of the many interesting points of cross-examination which forced FDA to agree that use in the perforators is within the intended use statement of the labeling.



Q. [Vascular defense counsel] All right. And if we go to the third page, so this is the new indications for use statement that was cleared by FDA, correct?
A. [Neil Ogden, FDA] Yes.
Q. And if we look at the first part, it refers to the ablation of soft tissue, correct?
A. Yes.
Q. And you'd agree that the veins are soft tissue, correct?

A. Yes.
Q. The great saphenous vein is made up of soft tissue?
A. Yes.
Q. Correct? The short saphenous vein is made up of soft tissue, correct?
A. Yes.
Q. Perforator veins are made up of soft tissue?
A. Yes.
Q. And tributary veins are made up of soft tissue, correct?
A. Yes.
Q. The second part of this clearance refers to varicose veins, correct?
A. Yes.
Q. The great saphenous vein can be varicose, correct?
A. Yes.
Q. The short saphenous vein can be varicose, correct?
A. Yes.
Q. Perforator veins can be varicose, correct?
A. Yes.
Q. Tributary veins can be varicose, correct?
Yes.
Q. And this clearance has been in place since March 26th, 2008, correct?
A. Correct. But nowhere in the indication for use does it say "perforator or tributary veins."
Q. You'd agree with me that perforator and tributary veins can be varicose, right, Mr. Ogden?
A. Yes.
Q. And the clearance says "varicose veins," correct?
A. Correct.

This is the same parsing of words FDA uses today in 510(k) labeling negotiations. ***FDA is fond of clearing devices that purport to be used for everything, but can be promoted for nothing.*** FDA believes that any

potential new indication for use must come back to the Agency for an additional clearance for which FDA often asks for more data. FDA frequently interprets the definition of "general versus specific intended use" so narrowly that FDA often considers new indications for a 510(k) device to be a new intended use. This is in contravention of the specific intent of the Congress. See our Client Alerts on "*Clearing Your Indications for Use: Staying Under the Umbrella of Intended Use*," and "*FDA's Interpretations Of General vs Specific Use—Through The Eye Of A Needle*" click here.

FDA can no longer avoid the 1st Amendment protection of truthful speech either. The FDA is under siege and has a bad track record with 1st Amendment cases. The 1st Amendment allows for truthful speech even if it addresses off-label uses. We believe today that the holdings in the 1st Amendment cases of *Washington Legal Foundation (WLF)*, *Sorrell v. IMS Healthcare, Inc. (IMS)*, *Caronia*, *Amarin* and *Pacira* cases challenge the conventional wisdom that FDA can regulate off-label speech to the extent it has, but FDA has not conceded that fact. These cases have found that the government has not used the least restrictive means to regulate protected commercial speech. ***These judicial decisions require management to rethink how it wants to approach commercial discussions regarding off-label use/claims about approved/cleared drugs and medical devices.***

The court in *Amarin* specifically rejected the idea that FDA can prosecute a manufacturer for speech that FDA admits is truthful and not misleading, simply because that use is not approved/cleared by FDA. The *Amarin* decision reminds us of a famous quote made by Judge Royce Lamberth in one of his *Washington Legal Foundation* (off-label dissemination) decisions where he matter-of-factly stated the following:

> In asserting that any and all scientific claims about the safety, effectiveness, contraindications, side effects, and the like regarding prescription drugs are presumptively untruthful or

misleading until the FDA has had the opportunity to evaluate them, FDA exaggerates its overall place in the universe.

Ironically, Judge Lamberth was the trial judge in the Howard Root/Vascular case.

The Agency has had many 1st Amendment losses in recent years and they are holding on to distinctions in the way they interpret the law which makes sense to no one—least of all physicians, judges and lay people serving on juries. See our Client Alert on the *Amarin* and *Pacira* cases click here. Yet the machinery of government and the overbroad positions it takes inspires great fear and chills much lawful behavior.

FOUR IMPORTANT TAKEAWAYS (AMONG MANY) FROM THIS CASE

The Government's continuing focus on "conduct" versus speech. Before the Root/Vascular trial commenced the defense brought a motion *in limine* (to limit evidence) to set ground rules for trial regarding the First Amendment free speech issues. Vascular cleverly moved to exclude all truthful speech from the trial. This would have forced the court to consider all the evidence about to come into the trial and to exclude it if it could be viewed as truthful speech because truthful speech is First Amendment protected and should not serve as the basis for a criminal adulteration and misbranding case.

While Judge Lambert dismissed the motion, it accomplished two things. First, it made the court focus in closely on the First Amendment defense issues. Second, it forced the government to disclose and elaborate on its theory of the case. The government in previous cases around the country had been losing these 1st Amendment free speech cases so the government began to argue that they were not prosecuting speech, rather "conduct." This theory had been rejected by many courts but mostly from the Federal

Court for the Second Circuit and this case was being held in Texas, the Fifth Circuit.

Here is the type of conduct the government believed led to its criminal adulteration and misbranding case without relying on any speech. This is taken straight from the government's brief (emphasis added in bold and italics):

> Rather than promotional speech to doctors, the United States will rely on the following conduct to prove the intended use of the devices:
>
> 1. ***Defendants' decision to launch*** a special kit designed specifically for perforator veins in response to a competitive threat (establishing intended use before any speech to a doctor even occurred);
> 2. ***their manufacture of that kit*** with perforator-specific modifications (manufacturing process for a device is not speech);
> 3. ***their application to the FDA for clearance*** to market that use (an FDA notification is a legal act and does not contain any speech to doctors);
> 4. ***their investment in a clinical trial*** for the purpose of gaining that clearance (no promotional communication to doctors occurred as part of this trial);
> 5. ***their decision to launch*** the product without clearance while adding new, deficient directions for perforator use to the labeling (Defendants do not argue that such instructions are protected speech);
> 6. ***their efforts to defraud the United States by concealing and lying about their perforator sales activity*** (fraud-based crime not protected);4

The interesting thing about this theory is that none of the "conduct" really becomes actionable until there is speech/communication made to the world outside the company to effectuate the conduct. It will be interesting, and doubtful, to see if a court someday will buy this fanciful theory. Judge Lamberth (the judge in this case) once opined, in the famous *Washington*

Legal Foundation (WLF) case that the regulation of marketing and promotional activities is regulation of "conduct" only "to the extent that moving one's lips is 'conduct,' or to the extent that affixing a stamp and distributing information through the mails is 'conduct.'" *Washington Legal Foundation v. Friedman*, 13 F. Supp. 2d at 59 (D.D.C. 1998). But the Court never had to make a decision on the conduct vs speech issue because the jury unanimously acquitted the defendants.

The jury instructions recognize off-label promotion for the first time. What is amazing about this case is that right before the trial started the government had to deal with both the *Amarin* and *Pacira* cases which broadly stand for the proposition that the government cannot regulate truthful speech about off-label uses. This has permitted the industry to toy with the idea that promotion of off-label uses, if put into proper context through appropriate disclosures and disclaimers, may be lawful. In the jury instructions, the government actually acquiesced to this unbelievable (for the government) jury instruction (emphasis added in bold and italics):

> Doctors may use medical devices that have been approved or cleared for one use for a different use that has not been cleared or approved by the FDA. This is often to as unapproved use or off-label use. This is not illegal. ***It is also not a crime for a device company or its representatives to give doctors wholly truthful and non-misleading information about the unapproved use of a device. If you find that VSI's promotional speech to doctors was solely truthful and not misleading, then you must find the Defendants not guilty of the misbranding offense.***

We assume the jury believed the speech was truthful as well as on-label.
It is time for FDA to rethink how it interprets general vs specific use and when new 510(k)s are required for new indications. The fact Vascular sought to "clarify" this use with FDA by proactively filing a 510(k), does not

change the analysis of whether the law required a 510(k) submission for this use. The bottom line is that the original clearance clearly encompassed this use and Vascular should not have had to submit a 510(k) to obtain it. But that is the dilemma in which industry finds itself. Industry often believes the use of its product is on-label and comfortably within the cleared general intended use statement, but is not sure whether FDA will agree or not. As such, they can market the product and face the prospect of a possible FDA warning letter or go to FDA and ask for an additional clearance knowing FDA will most likely either 1) agree it is a new indication and require a lot of data for clearance (and suggest a Pre-Submission meeting), or 2) state it is a new intended use altogether and require a de novo or PMA submission, again with a lot of data.

The Agency lost another one. This is the first in the hands of a jury. The others were court decisions. Where FDA goes from here will be interesting. We know FDA was regrouping last summer and determined to develop a new policy on off-label communication. Had they not been so stubborn and so slow to recognize how wrong they have been in this First Amendment arena, they could have gotten out ahead of industry with a proposal that may have been palatable to industry and would have allowed them to retain some authority, albeit beyond its actual authority. But the cat is out of the bag. Industry has the upper hand with all of these judicial decisions and jury verdicts now behind them. The promotional landscape will forever be changed—for the better. ***We now seem to have a concept we can call "off-label promotion."***

Author's note: I interviewed Howard Root before writing this **Client Alert**, and these represent my thoughts not his, but I asked him for one quote I could use. In typical Howard Root fashion, reflecting on the fact that Vascular won without even calling a single witness, he said "***This is the most decisive victory since Operation Desert Storm, at only slightly greater expense."***

It took twenty-five million dollars ($25MM) to defend this case. This case is a great victory for Howard Root, Vascular Solutions and the industry, but a sad commentary on the power of the government. It frequently operates out of positional strength and not on the strength or persuasiveness of its ideas and statutory/regulatory interpretations.

DuVal & Associates
Drug, Device and Food Law

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