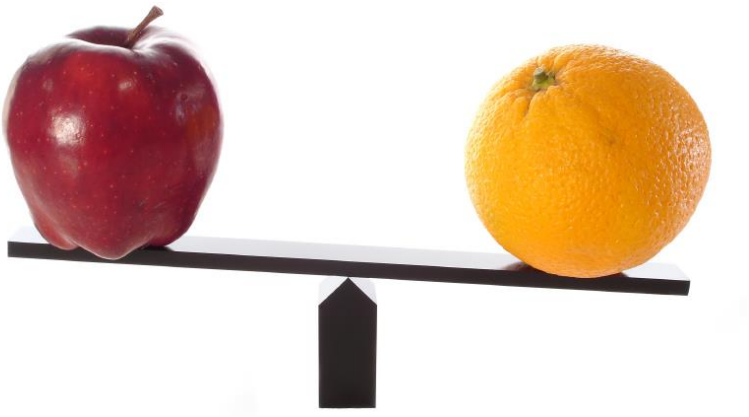
DuVal Client Alert

Passing on Tribal Knowledge of FDA Law

The 5th Client Alert in Our Series on 510(k)s



Fruit	•	Same
Used for food	•	Same
Round in shape	•	Same
Comes from trees	•	Same
Has core with seeds	•	Same
Exterior skin edible	•	Different (edible, not tasty)
Contains vitamin C	•	Same

Addressing Technological Characteristics in Your 510(k):

Finding the Similarities Between Apples and Oranges

This is the next Client Alert in our series on drafting and filing strategies for 510(k)s. The strategies we share in this series are borne out of our experience in counseling clients on how to ensure their 510(k) is an advocacy document that garners the clearance they seek. Here are the previous Client Alerts in this 510(k) series:

- 1st—"Dotting the I's and Crossing the T's: Withstanding the 510(k) Acceptance Review;"
- 2nd—"Seven Quick Tips for Successful 510(k) Submissions--do you need our help with your next submission?;"
- 3rd—"Choosing the Proper Predicate Device(s): Comparing Apples to Oranges;" and
- 4th—"Clearing Your Indications for Use: Staying Under the Umbrella of Intended Use."

Find these prior Client Alerts at our website www.duvalfdalaw.com

In this Client Alert, we share our tribal knowledge for making a cogent argument that your device shares the same technological characteristics as your chosen predicate. We share what not to do when depicting your device in a submission and how to persuade FDA to your position. We alert you to arguments FDA often makes to suggest your device has different technological characteristics and does not belong on the 510(k) path. We arm you with potential responses to FDA. We help identify and emphasize the technological similarities your device shares with the predicate device so that you can remain of the 510(k) path. ***At the end, we share with some tips to be creative and advocate for your position that your device has the same technological characteristics***.

As we conclude our series, we will share insights from our negotiations with the Agency on such matters as whether a device raises different questions of safety and effectiveness in comparison to a predicate device which is intimately related to the issue addressed in this Client Alert on technological characteristics. In a future Client Alert we will also discuss the quantum and quality of data that should be submitted for clearance and where to push back on the Agency.

EXECUTIVE SUMMARY

Finding the similarities between apples and oranges

One of the main tasks in your 510(k) submission is comparing the technological characteristics of your device to your chosen predicate device. Like the issue of whether a device has the same intended use, FDA is more restrictively interpreting when a device has the same technological characteristics. When that happens, the device becomes ineligible for the 510(k) path. Your assignment, should you choose to accept it, is to convince FDA of the "sameness" between your device and the

predicate. You must persuade FDA that your device is like the predicate even when there are some differences. FDA must be convinced that those differences are not so great that the device is deemed to have technological characteristics that are different. "It's like comparing apple to oranges," the well-known idiom, implying the comparison is to things that are quite different; except the exercise here is to find the similarities between apples and oranges. This requires making more than a superficial comparison. It requires finding the essential nature of the technology and whether the individual technological characteristics accomplish the same therapeutic mission as the predicate, possibly in a slightly different way, or do they do more or something different such that it really is a different device. It often takes a mindset from the reviewer that is looking for technological similarities rather than the differences from the predicate.

When the sponsor uses creativity and solid logic in making the comparison, it is amazing what similarities can be found. For example, both an apple and an orange are fruit. They both are nutritious. The both have seeds. The edible and best part of both fruits lies beneath the outer skin. The apple skin, however, is edible and the orange peel may not considered edible per se, but actually it is. It's just not as tasty as the apple peel. It's sort of neutral in terms of taste. Both have vitamin C and so both are good for you. So the differences in the outer skin and differences in vitamin content do not diminish the fact that both are nutritious and provide sustenance. This is true even though the way each fruit provides nutrition is different (the mechanism of action if you will). Both still provide energy for the body and boost the body's immune system. The bottom line is the sponsor must convince the Agency that the similarities outweigh the differences and the essence of the fruit (or device) is the same.[1]

It must be remembered that even if the Agency finds that a device has different technological characteristics, it is still allowed to stay on the 510(k) path, if the differences do not raise different questions of safety and effectiveness. This Client Alert is focused on when a medical device has or does not have the same technological characteristics. The topic/discussion of whether a device raises different questions of safety and effectiveness is the subject of our next Client Alert.

---

[1] There have been published studies (albeit tongue-in-cheek) that conclude apples and oranges share extensive similarities and can be scientifically and defensibly compared. Although this is seemingly outside the scope of this Client Alert, it nonetheless demonstrates that stating the obvious, overlooked traits and having a little creativity can help you make any defensible argument about similarities. See e.g., see James Barone, "Comparing apples and oranges: a randomized prospective study," 321 Brit. Med. J. 1569, 1569–70 (2000) and Scott A. Sandford, "Apples and Oranges - A Comparison," 1 AIR, Vol. 1, No. 3 (1995).

ANALYSIS

The 510(k) pathway was designed to allow innovation

The 510(k) pathway is designed to be sufficiently flexible to accommodate technological innovation and yet allow for the subject device to be substantially equivalent to predicate devices. As such, 510(k) devices are allowed, even expected, to have some differences from the predicate, even though they must be "substantially" equivalent. Over time the 510(k) process accommodates significant changes over the predicates devices that may even go back decades even though each incremental change vis-a-vis a given predicate may not be nearly so great. As FDA has said in its new (2014) guidance document on substantial equivalence (510(k)) determinations:

> ***A new device does not need to be identical to the predicate device for it to be found substantially equivalent to the predicate device. In FDA's experience, it is rare for a new device to be identical to a predicate device***. Given the diversity of technologies evaluated under this review standard, ***this guidance adopts a flexible approach*** to determining "substantial equivalence" to accommodate evolving technology while maintaining predictability and consistency to promote confidence among device developers, practitioners, and patients.
>
> ...
>
> ***Devices reviewed under the 510(k) program commonly have different technological characteristics from their predicate device***(s); however, FDA rarely makes a finding of NSE at Decision Point 4.

The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]," dated July 28, 2014 (hereinafter the "New 510(k) Guidance") (emphasis in bold and italics added).

Companies today are submitting combinations such as 1) ***existing materials*** in different anatomical and/or therapeutic uses; 2) ***existing engineering concepts*** in different anatomical and/or therapeutic uses; 3) ***combinations of materials and engineering concepts*** (in new anatomical and/or therapeutic uses); 4) ***the addition of*** antibiotics, antimicrobials, OTC drugs, etc.; and 5) many others. All of these new and interesting combinations are not necessarily novel in the PMA sense, but do challenge the FDA and the 510(k) framework in that they are not conventional, generic-like copies of existing devices. But, as stated above, the 510(k) program is

designed to accommodate technological advances and hence the term "substantially" equivalent. The labeling and the technological features need not be identical. Still, these changes can raise interesting questions upon FDA review.

FDA's own guidance documents recognize that incremental changes, even advantages, to products occur as technology improves and new ideas are brought to bear upon pre-existing product ideas. Sometimes the predicate landscape demonstrates the progression or evolution that the devices in the predicate family have made. FDA has pejoratively called this "predicate creep." But predicate creep is a good thing, not a bad thing. It means technology is progressing and naturally evolving; which is what the 510(k) program was designed to foster, as long as that technology progression continues with a device in an acceptable, incremental technological evolution. Very often devices show themselves to be valuable and reasonable evolutions in the predicate family.

Here are some of the issues we see with FDA's application of the "same technological characteristics" criterion. First, the Agency often searches for differences and then categorically states the device has different technological characteristics without making any attempt to justify its conclusion. Second, the Agency has taken a markedly different tack in its new guidance on how to analyze when a subject device has a technological characteristic from a predicate. FDA's new approach differs greatly from FDA's old guidance and we believe it is not faithful to the statute or regulations. We address both below.

FDA often finds differences without articulating why

If FDA could simply say, with respect to any device, that "it **thinks** this device is fundamentally different than the predicates because it has different technological characteristics and is ineligible for the 510(k) path," what would ever stand in FDA's way from saying that for any device it did not want cleared as a 510(k) device? How do companies practically refute an unarticulated, unsupported statement? The check on FDA's unbridled discretion, its bare conclusion, is the standard that Congress has provided, i.e. whether the device actually has different technological characteristics. This is to be guided by the flexibility with which the 510(k) was designed. The older guidance documents provided industry and FDA with some analytical tools to address that interpretive problem. Your job is to convince the FDA why the devices share the same technological characteristics.

FDA's older guidance emphasized the bigger picture, i.e. the "consequentiality" of the difference

In older FDA guidance (the K86-3 Blue Book Memo which, sadly, has been decommissioned), FDA stated that in determining whether a device has new technological characteristics, FDA should focus on changes that are "consequential" and require them (and only them) to be addressed:

> Thus, from a scientific perspective, to determine which technological changes are "consequential," the Center considers whether:
>
> - The new device ***poses the same type of questions about safety and effectiveness*** as a predicate device;
> - There are ***accepted scientific methods for evaluating whether safety or effectiveness has been adversely affected*** as a result of the use of the new technological characteristics; and
> - There are ***data to demonstrate that new technological characteristics have not diminished safety or effectiveness***.

See 510(k) K86-3 Blue Book Memo at 7 (emphasis added).

The focus was pragmatic and took an overarching, common sense view of what is a new technological characteristic. We will juxtapose that below with FDA's new granular approach that requires a deep dive into every conceivable difference between the subject and predicate device. This approach lends itself much more readily to a finding of different technological characteristics.

So taking the criteria set forth in CDRH's Blue Book Memorandum, we must look at any given product and the Blue Book questions holistically and ask "Are the changes really 'consequential?'" As FDA has (in the past) stated:

> In taking this approach, ***the Center focuses on the technological differences that are medically and scientifically significant and avoids the difficulties that would arise from a mechanistic application of rigid formal criteria*** to the wide variety of substantial equivalence questions posed by new devices proposed for marketing under a 510(k). Substantial equivalence determinations of necessity ***require the Center to exercise reasonable scientific judgment***.

See 510(k) Blue Book Memo at 7.

The problems we see are threefold. First, FDA often is quite mechanistic in its view of technology. Novel improvements may be novel from a patentability perspective, and they may be novel in approach from a predicate family standpoint, even though they are SE. FDA needs to celebrate modest technological advancement, not fear it. **Second, even though there may be changes, they are not medically**

and scientifically significant. The changes may help the physician better use the device or deploy it. The device may be less invasive for the patient. But such changes may not be medically and scientifically significant. They may be inconsequential. We implore the FDA to "exercise reasonable scientific judgement" rather than making a science project out of small inconsequential differences. If you look under a microscope long enough, you are bound to see differences, but are they consequential?

Third, FDA often confuses a technological difference with whether a device raises a different question of safety and effectiveness and this can get quite frustrating. FDA often will see a device they believe to be different from the predicate and FDA knows that it cannot be dismissed because it does not raise new questions of safety and effectiveness. In fact, the device will raise the same questions. Instead, FDA will contort its analysis to find the device somehow has different technological characteristics and/or raises new questions of safety and effectiveness. In any case, it is evident what is happening; FDA is once again applying definitions in a manner that forecloses the 510(k) pathway in favor of the de novo path; simply because they can.

FDA's new guidance emphasizes the granular picture, i.e. small differences and seems to require a "PMA-like" review

In FDA's New 510(k) Guidance it takes an entirely different approach from the past. Rather than looking at whether changes are "consequential" and exercising "reasonable scientific judgment" and avoiding a "mechanistic application of rigid formal criteria," FDA is getting more granular in its approach to 510(k)s. The New 510(k) Guidance is disappointingly microscopic in how it now reviews the issue of whether a device has the same technological characteristics, which belies the more generous, common sense interpretations it has historically been given.

The new standard, i.e. whether a "different question of S&E" was or was not applicable in the 510(k) for the predicate, should not be the standard. In most cases the question was **not** considered in the review of the predicate—and the default position becomes an NSE determination. The actual standard is not whether the question was raised or not, but whether it is a different question of S&E and if data can answer those questions. The new standard seems to contradict the concept of "reference" device which allows FDA to borrow knowledge from its vast repository of institutional knowledge and apply it to the device (the subject device) under consideration.

The new standard also contradicts the approach taken in K86-3, i.e. to consider whether the change is "consequential" and focuses merely on the presence of a change—which all 510(k)s have—and not the importance of the change and whether it changed the essence of the device.

We remain concerned about the level of detail FDA will require for a submission by following Steps 1-3 of the "Technological Characteristics" part of the submission. These "steps" FDA requires will produce a far more detailed review than was ever intended for a 510(k). The steps for determining whether technological characteristics (TCs) are the same are briefly outlined below. While the progression of the steps seems logical, the application of them can get quite detailed and tedious. This favors many opportunities for reviewers to notice granular differences that should not matter in the overall scheme of things (i.e. the inconsequentiality of them):

> **Step 1—Identification of TCs of the New and Predicate Device**—the 510(k) should include: an overall ***description of the device design*** with "significant features" having a "clear purpose" for each feature within the context of the overall design and intended use. It should also include ***materials*** including detailed chemical formulations, additives like coatings or surface modifications, processing of the material and the physical state of the material, etc. It must also address ***energy sources*** delivered to the device and patient. Finally, it must include ***other key technological features*** like software/hardware features, density, porosity, degradation characteristics, nature of reagents (recombinant, plasma derived, etc.), principle of the assay method, etc., that are not explicitly included as part of the materials, design or energy source characteristics.
>
> **Step 2—Identification of Differences in TCs Between the New and Predicate Device**—involves a granular line-by-line material comparison of these characteristics to identify any differences; this may involve a comparison of detailed specifications as well as a comparison of the system-level technological characteristics of the devices.
>
> **Step 3—Determination of Whether Differences in TCs Raise New Questions of S&E**—FDA is looking for differences that that were not applicable in the 510(k) for the predicate; a "different question of safety or effectiveness" is a question raised by the technological characteristics of the new device "that was not applicable to the predicate device, and poses a significant safety or effectiveness concern for the new device."

The information FDA is looking for appears to resemble the level of granularity required for a PMA, not a 510(k). This is one of the changes that at first blush may appear benign, but may fundamentally alter the way in which 510(k)s are supposed to be reviewed, i.e. with a broader review of "substantial" equivalence, acknowledging that devices need not be identical to be cleared. It's like finding that this tree is different from that tree (because of granular differences), rather than saying this tree looks like it belongs in this forest (the predicate family).

We are also concerned that significant features of the new device should have a "clear purpose" which allows the Agency to avoid a broader more pragmatic review and engage in a mechanistic application of whether the device has the same technological characteristics and whether it raises different questions of safety and effectiveness. At first blush, this "clear purpose" language seems innocuous; but again, it is introducing a level of granularity not previously contemplated for the 510(k) program. Often an existing device may have features that may be put into play when future 510(k)s are submitted for new labeling, Even though the current 510(k) submission is not requesting that broader "assumed" labeling. It is inappropriate for FDA to assume an unstated claim for use. FDA must accept at face value the claim being sought and limit its review to that claim. FDA must limit its request for information to whether the device has 1) the same intended use, 2) same technological characteristics, and 3) if there are different technological characteristics, do they raise different questions of safety and effectiveness. The Agency by requesting a "clear purpose" may essentially be assuming an unstated use which is prohibited by law under 513(i)(1)(E).[2] The Agency cannot do (or ask) indirectly, what it is not allowed to do directly.

The FDA also asks whether a new technological characteristic raises a different question of safety and effectiveness which was not considered in the review of the predicate. That is not the proper standard because frequently questions not previously raised by FDA in the past predicate reviews (or previously not even deemed important by FDA), does not mean it is a different question just because FDA now considers it important today. So in most cases where new indications for use or technological characteristics are being pursued, the same questions of safety and effectiveness of course may not have been considered, but often they are not so different as to make them ineligible for the 510(k) path. If this becomes the new standard, we will have far fewer 510(k)s eligible for the 510(k) path today because

[2] See Section 513(i)(1)(E), 21 U.S.C. § 360c(i)(1)(E), which states in part, [a]ny determination by the Secretary of the intended use of a device ***shall be based upon the proposed labeling submitted*** in a report for the device under section 360(k) of this title." [Emphasis added.] FDA cannot assume an unstated use in reviewing a 510(k) application.

the current (risk averse, academically-oriented) FDA often considers even the most inconsequential issues, not worthy of practical consideration in the past, as vitally important today (and therefore as obstacles to clearance).

Overall we seemed to have lost the "consequentiality" and practicality of the 510(k) standard of review found in the K86-3 guidance that is being replaced by the New 510(k) Guidance. FDA's interpretations today allow it to parse rules in its favor to i) bounce the device off the path into one of its unofficial "diversion" programs, i.e. the de novo path or a Pre-Submission meeting, and/or ii) ask for any and all data FDA wants. Being facetious, if we were to rewrite the K86-3 Blue Book Memo to reflect how the Agency could (unchecked) proceed going forward, this is how we would **not** want it to look like (additions in red, deletions in green):

> In taking this approach, the Center focuses on the technological differences that are medically and scientifically ***in***significant and avoids ***embraces a overly-technical reading of the law*** the difficulties ***that may lead to*** would arise from a mechanistic application of rigid formal criteria to the wide variety of substantial equivalence questions posed by new devices proposed for marketing under a 510(k). Substantial equivalence determinations of necessity require the Center to ***be risk averse and*** exercise reasonable ***needlessly granular*** scientific ***curiosity*** judgment ***disproportionate to a moderate risk device***.

We do not want to lose the practical, less mechanistic spirit of K86-3, which could happen if: i) inordinate granularity is added/required to the information being requested and examined, ii) the consequentiality of the changes are not considered with pragmatism, iii) young, inexperienced reviewers are not provided with appropriate direction, and iv) branch chiefs fail to control their reviewers' natural propensity to be risk averse.

The future is a matter of "administrative will"

It is a matter of mindset—does the Agency want to hinder or help new medical technology to the market place fulfilling the second half of its twofold mission statement, i.e. to help speed innovations to market? The regulatory interpretations will follow the mindset—the administrative will—to be collaborators, not obstructionists. It is critical that FDA continue to train, monitor performance, find ways to show the rest of the organization how decisions should be made, and explain when different decisions could have been made (especially when review staff are overturned). It would also help if FDA randomly and anonymously interviewed sponsors to understand their experience and concerns with the 510(k) process during

and after a review. Otherwise the Agency is only listening to itself. These measures will help ensure the transparency, predictability and reasonableness that the Agency desires. Risk averseness and inexperienced, impractical (academic) decision making that does not follow the statutory framework are still a problem for the Agency. We remain hopeful that the Agency experience is growing and getting better and more practical. We have a positive Agency example below.

Your job is to be creative and advocate for your position

Despite this guidance and the fact FDA review staff can, and often does, apply it with great impracticality and granularity, management often sees the light and gives broader more practical applications. Your job is to advocate and provide compelling reasons why you have the same technological characteristics.

We have worked on many positive examples where FDA used its "administrative will" to find that a device had the same technological characteristics where it could have found otherwise. In some 510(k) submissions we could imagine the myriad issues the FDA could have dreamed up, but instead concluded the device was within the overall concept/function of the predicate family despite its novel approach. We credit the Agency for interpreting the 510(k) program in the manner originally intended by Congress. The key to persuading FDA to your position is to be creative, tell your story and advocate for your position. We recommend the following:

1) **Start with a mindset of "sameness."** Do not try to sell your device to FDA, i.e. that it will change the practice of medicine, that it is superior to competitive devices, or that it is addressing an unmet clinical need. Sell the uniqueness of your device after clearance, once you are in the marketplace. Describe your device as having features and benefits that are essentially the same as the predicate. Keep your eye on what the essential functionality is and describe your device in those terms, i.e. that your device is within the overall concept/function of the predicate family despite its novel approach.

2) **Use a comparison chart to compare the features of your device with the predicate.** Don't hide anything from the Agency, but don't unnecessarily point out minute, inconsequential differences either; because your position is, or should be, that based on FDA's guidance that inconsequential differences do not matter in comparing technological characteristics.

3) **Think of the progression of the technology in the predicate family and make an argument that your technological differences are well within the scope and breadth of changes that have already taken place.** The 510(k) program is designed to be sufficiently flexible to accommodate technological innovation. Often the best proof of that is showing what changes FDA has accepted in devices cleared before your device. Demonstrate how your device fits within the evolution of technology in the predicate family.

4) **Use FDA's own guidance documents against them.** FDA has many guidance documents (old and new) where either the narrative or examples used therein help make the case that your technological characteristics are of the kind contemplated by Congress in the law (and Preamble), or by FDA in the regulations or guidance. Use them.

5) **Tell your story and make your case.** Your job is to persuade them. Remember the 510(k) is not just an evidentiary document, it is an advocacy document.

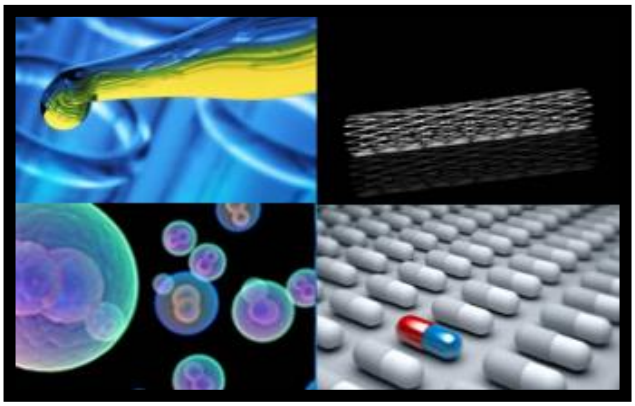
Certainly, the FDA today can go to great lengths to use Steps 1-3 in the New 510(k) Guidance to determine a device is NSE. Instead, we hope the Agency embraces incremental technological innovation and avoids "the difficulties that would arise from a mechanistic application of rigid formal criteria to the wide variety of substantial equivalence questions posed by new devices."

Need Assistance with Your 510(k)?

Do you need help presenting or understanding the implications in addressing technological characteristics in your 510(k)? Have you hit a roadblock with your 510(k) because of your new device's technological characteristics? Our firm routinely engages with clients regarding medical device submissions and appeals, including advising on regulatory strategy, counseling on regulatory and FDA matters, and providing general assistance with 510(k) submissions and Pre-Submissions. Watch for the next **Client Alert** in our series on 510(k) submissions. If you have any questions or would like more information about how we can help you with your 510(k), please contact us at duval@duvafdalaw.com// or by phone at (612) 338-7170.

CALL ON US FOR ASSISTANCE WITH YOUR REGULATORY NEEDS

DuVal & Associates is a boutique law firm located in Minneapolis, Minnesota that specializes in FDA regulations for products at all stages of the product life cycle. Our clientele includes companies that market and manufacture pharmaceuticals, medical devices, biologics, nutritional supplements and foods. Our clients range in size from Global Fortune 500 companies to small start-ups. As one of the only dedicated FDA regulatory law firms in the United States, our mission and absolute focus is providing our clients appropriately aggressive, yet compliant, guidance on any FDA related matter. We pride ourselves not only on our collective legal and business acumen, but also on being responsive to our client's needs and efficient with their resources. DuVal & Associates understands the corporate interaction between departments like regulatory affairs, marketing, sales, legal, quality, and clinical, etc. As former industry managers in the drug and devices spaces, we have been in your shoes. Our firm has extensive experience with government bodies. We understand what it takes to develop and commercialize a product and bring it successfully to the market and manage its life cycle. Impractical or bad advice can result in delays or not allow for optimal results; while practical, timely advice can help companies succeed. ***For more information, visit our website at www.duvalfdalaw.com or call Mark DuVal today for a consult at 612.338.7170 x1.***



To stop receiving Client Alerts, please reply to this email with the subject "Opt Out." To be added, please email **afeldkamp@duvalfdalaw.com** with your contact information.

DISCLAIMER: Material provided in Client Alerts belongs to DuVal & Associates and is intended for informational purposes only and does not constitute legal advice.