



510(k) Substantial Equivalence In Plain English — Part 1

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The 510(k), or premarket notification, process has been around since 1976, when it was introduced as part of the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act. In the nearly 40 years that have passed since its implementation, the 510(k) has become the most commonly used regulatory pathway for bringing new medical devices and diagnostic products to market in the United States.

Although it is a well-worn path, the 510(k) is poorly understood, in my opinion. This is evidenced by the fact that almost 75 percent of first-time 510(k) applications are initially rejected by the FDA — a major reason why the 510(k) review process is taking 114 days to complete, on average, in 2014.

The two most important components of a successful 510(k) submission are the substantial equivalence argument and the risk mitigation strategy. You can fill out all of the forms — you can dot all your i's and cross all your t's — but if you don't have a very strong substantial equivalent argument and a bulletproof risk mitigation strategy, you probably are not going to be successful in getting your submission cleared, and certainly not in the first review cycle!

This two-part article will focus specifically on the substantial equivalence component of 510(k) submissions, explaining what it is and how to establish it. It will also explore two recently issued FDA guidances related to substantial equivalence, and how they should influence your regulatory strategy.



What Exactly Is Substantial Equivalence?

Substantial equivalence is the crux of the medical device industry, because we all rely on it so heavily to bring our products onto the market under the 510(k). But how many really understand what it means? Before getting into the regulatory gobbledygook, I'd like to share a couple metaphors to help explain the concept of substantial equivalence.

Is a car substantially equivalent to a truck? If you want to bring a truck onto the market under the 510k, you could compare it to a car (i.e., predicate device), and the regulatory logic is quite simple. You want to emphasize the similarities and at the same time de-emphasize — or at least not draw attention to — the differences. So, you would emphasize that both cars and trucks are vehicles for transportation, both have wheels, both have internal combustion engines, both consume fuel, both travel on roads, and so on.

At the same time, we have to downplay the differences. Cars usually have four wheels, while trucks may have as many as 18 wheels. Cars usually burn gasoline or perhaps electricity; trucks often burn diesel fuel. Cars are usually designed to carry people and maybe a small amount of cargo, and trucks, on the other hand, carry much more cargo.

We need to acknowledge the differences if they are to our advantage and show that, although they exist, they will not impact the safety, efficacy, or performance of the device. If the differences are not to our advantage, however, we should not bring them up prophylactically but be prepared to respond to them if and when we are asked. This gets into much more sophisticated regulatory strategy, but to use another metaphor this is a poker game, and just because you know the rules does not make you a good poker player!

Another very simple metaphor that everybody can relate to: apples and oranges. Is an apple substantially equivalent to an orange? Well, once again, you want to underscore the similarities: They are both fruits, they both grow on trees, they both deliver calories and nutrients, they both have skin, they both have seeds, etc. But you also want to minimize the differences: they are different colors, they have different nutritional content, they grow on different trees, and so on.

Why use simple metaphors like these? Because Einstein said if we can't explain something simply, we don't understand it well enough. The same principle applies to establishing substantial equivalence for more complicated medical devices, like a vena cava filter or a hip implant. Emphasize the similarities; de-emphasize the differences. I know this sounds like a very basic concept, but I am consistently surprised by how many companies fail to utilize it.

The regulation says that in order to use the 510(k) pathway, there must be a predicate device. But the regulation does *not* say how close the predicate device must be to the new device — nor should it! That is up to the manufacturer and the FDA to negotiate by working together. Is a car close enough to a truck? How about comparing a Honda CR-V to a Toyota RAV4? That is closer yet, but is it close enough? How about instead of comparing an apple to an orange, we compare a red apple to a green apple? In general, the closer the comparison, the easier it is to make the substantial equivalence argument. But where do you draw the line, and who decides?

Recent FDA Guidance And Its Impact On Substantial Equivalence

In order to provide industry with some much-needed clarity regarding the premarket notification process, the FDA's Center for Devices and Radiological Health (CDRH) has issued several 510(k)-related guidances over the past several months. In the next section – and Part 2 of this article – we will look at two specific draft guidances that could have implications in formulating substantial equivalence arguments.

Benefit-Risk Factors to Consider When Determining Substantial Equivalence in Premarket Notifications [510(k)] with Different Technological Characteristics

Issued in mid-July, this [guidance](#) emphasizes – and this is right out of the original Court of Federal Regulations – that in order for a device to be shown substantially equivalent to its predicate, it has to have either:

1. The same intended use as the predicate and the same technological characteristics, or
2. The same intended use and different technological characteristics.

What does this mean? I have no idea, but I use such regulatory ambiguities to my advantage all the time! I don't think anybody really understands it completely. It seems to suggest that as long as you get to where you want to go (intended use), it doesn't matter how you get there – whether you use the same technological characteristics in your device or different technological characteristics.

Once again, let me use a very simple metaphor. Say you wanted to get from Boston to Los Angeles. You could drive a car there, though it would take you a couple of days to do it. You could also fly an airplane from Boston to Los Angeles, which would be much quicker and more efficient. In the end, either method of transportation will get you to Los Angeles. So by that regulatory logic, a car is substantially equivalent to an airplane, because although we use different technologies, we end up in the same place (i.e., the intended use).

That's exactly the regulatory logic behind the substantial equivalence argument in the 510(k). But where do you draw the line? You could also fly a helicopter from Boston to Los Angeles. You could ride your bicycle. You could take a cruise ship through the Panama Canal. You could even take a UFO from Boston to Los Angeles. Does that mean all of these modes of transportation are substantially equivalent? As long as you get to Los Angeles, it's the same intended use, so can the technology can be the same or different?

This ambiguity is one of the reasons why the 510(k) has become so controversial in the eyes of some people. As a matter of fact, the Institute of Medicine (IoM) came out with a report in 2011 recommending that the 510(k) should be totally thrown out. I strongly disagree with IoM's position – that would be throwing the baby out with the bathwater. I think the 510(k), and more specifically the substantial equivalence regulatory logic, is a valid path to bring medical devices onto the market when used properly. But like any tool, it can be misused. The key to making this or any regulation work is not to focus on the regulation, but rather the negotiation between the manufacturer and the FDA – that is what will ultimately determine how long a submission will take and whether it will be successful.

We'll delve into the use/misuse of regulation further in Part 2 of this article, as we look at a second draft guidance and discuss potential CDRH changes to so-called split-predicate approach to establishing substantial equivalence.

Dr. Drues will be teaching an online course called [The Premarket Notification/510\(k\) Submission: Using Substantial Equivalence to your Advantage](#) on October 16, 2014, at 1:00 pm. The course will go into much more detail on the topic of substantial equivalence, using actual medical device case studies to illustrate these concepts.