MEDICAL DEVICE & DIAGNOSTIC INDUSTRY

Third-Party 510(k) Review: A More Attractive Alternative?

Now that user fees have increased, device makers are advised to give third-party reviewers a second look.

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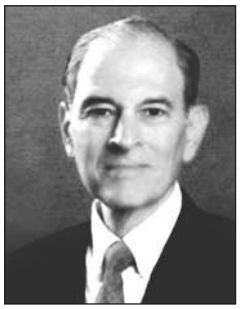
Many device companies have opted for third-party 510(k) reviews to help get their products on the U.S. market months faster. Now, with FDA increasing its review fee from $2187 to $3480 ($2784 for small businesses), effective October 1, 2003, third-party review becomes an even more attractive alternative. The reason? Third-party submissions are completely exempt from the fee.



The third-party review program began in 1996, with just 15 device types eligible; predictably, few companies took advantage of it. Today, most 510(k)s can be reviewed by third parties, with 14 accredited organizations situated around the world. The program allows sponsors to submit their eligible 510(k) applications to an approved third party—an "accredited person," in FDA parlance—rather than directly to FDA. The third-party organization conducts the primary review, which is where months' worth of time can be lost at FDA. When the third party is satisfied that the 510(k) has demonstrated substantial equivalence (i.e., the criterion for clearance), it sends the complete 510(k), together with its review documentation, to FDA for a final decision—which comes quickly.

Because the third parties receive no FDA funding, they have always charged a fee for 510(k) reviews. Today, their fee has effectively been reduced by FDA's charge for direct 510(k) submissions. Even so, the "reduced" fee is but one reason for companies to use third-party review; the major advantage is that it can help a company market its new product months sooner. FDA has estimated that third-party review cuts an average of two to three months off the time to clearance, compared with similar 510(k)s submitted directly to FDA. For some product categories, where FDA staff is overburdened, typical time savings are much greater. Consider the advantage to the manufacturer of a large imaging system of even one or two additional early sales. Or, the benefit of being able to plan to introduce a new product at a major show, rather than wondering about and waiting for the FDA decision to come, and feeling helpless to speed it up.

How Third-Party Review Works

Submissions eligible for third-party review are generally those for Class I and Class II devices requiring 510(k) clearance that are not implantable, life-sustaining, or life-supporting, and where substantial equivalence can be demonstrated without the need for human clinical data. Many reprocessed single-use devices are eligible, as well. If a submission is eligible for third-party review, the sponsor contacts one or more accredited persons and obtains proposals. FDA maintains a list of accredited persons—as well as a detailed list of device types eligible for third-party review—by three-letter product code, on its Web site, www.fda.gov/cdrh/thirdparty. Not all third parties are accredited for all product types.

For many kinds of devices, FDA has issued guidance documents regarding the content of a 510(k) submission; in fact, only devices covered by such guidances were initially included in the third-party review program. This restriction has been removed and devices otherwise eligible for third-party review, but for which a specific guidance document does not exist, are designated as Expansion Pilot devices. For these products, the third party is required to contact FDA prior to initiating its review, to discuss specific areas that the reviewer should address. This contact is not required before a third party reviews subsequent submissions for the same product category.

Whether it is reviewed by FDA or by a third party, a 510(k) must demonstrate substantial equivalence to a predicate in the same way. Where the reviewer—FDA or third-party employee—perceives a deficiency, additional information will be requested of the sponsor. What is different, however, is the timing. Because companies pay the third parties a fee for their service, they are in a position to demand speedy reviews, something they cannot do with direct submissions to FDA. For example, when a third-party reviewer requests additional information, the sponsor can ask that other aspects of the review continue in the interim; the same cannot be asked of an FDA reviewer. This example points to another benefit of third-party review—it's

friendlier. The individual reviewer is usually more readily accessible and amenable to discussion at a third-party organization than at FDA.

Once the third party has completed its review, it sends two copies of the complete 510(k), along with any additional information, its review documentation, and its recommendations, to FDA. There, the submission bypasses the time-consuming primary review and goes directly to the branch chief's desk. The branch chief can either issue a clearance letter or request additional information from the third party in order to find substantial equivalence. By law, this must happen within 30 days; in practice, it has been happening in 15 days or less. If additional information is requested, the third party passes the request along to the sponsor, who either provides it or explains why additional information should not be needed.

When additional information has been requested by FDA (the branch chief, in the case of third-party submissions), there is an important difference between third-party submissions and those sent directly to FDA. Either way, the submission is placed on 30-day hold. However, once the new information is provided, a third-party 510(k) submission goes back into the fast track, whereas a direct FDA submission can go into the usual 90-day review track.

Who Should Consider Third-Party Review?

There are some products for which third-party review is particularly advantageous; these tend to be complex, high-ticket equipment, for which the potential sales benefits of earlier market introduction will easily overcome the third-party review fee. (Of course, many sophisticated devices are not eligible for third-party review, often because the 510(k) requires human clinical data. The detailed list of eligible devices, on the FDA Web site, is helpful in determining eligibility. When a particular submission requires human clinical data, however, it's ineligible for third-party review, even if it's on the list.)

Another group of products especially suited to third-party review are those for which FDA review times are unusually long. Because of personnel shortages, some FDA branches are slower than others, even on simple reviews. Information on FDA review times is available on the Internet—see sidebar for guidance on finding it. If FDA typically takes just a month or two to review 510(k)s for a certain product type, the time saved with a third party might not be significant. On the other hand, a company may not want to play the odds with a particular submission, and it might choose to pay a third party for more-assured speed.

Conversely, there are eligible devices for which third-party review is not suited. Mass-produced me-too products generally don't generate sufficient sales to recoup the third-party fee unless there's a major contract contingent on quick 510(k) clearance. Also, submissions that qualify as special 510(k)s will receive a 30-day response directly from FDA, so it would be counterproductive to use a third party for those reviews.

Conclusion

Companies that have used third-party 510(k) reviews are almost universally sold on the concept, getting their clearance letters just weeks after the reviews begin. Yet, the vast majority of 510(k)s that could be reviewed by third parties are still being submitted directly to FDA. Some companies may be unnecessarily concerned about confidentiality. Accredited third parties are required to maintain the same confidentiality, with respect to submissions, as are FDA staff members; they may discuss confidential information only with FDA and with the sponsor. Other companies may not have used third-party review simply out of habit, or because it introduced an additional contractual agreement into the process. Finally, some regulatory consultants may hesitate to recommend third-party review, fearing competition for future business; they should recognize that accredited third parties are not permitted to offer regulatory consulting or help prepare 510(k)s.

Perhaps the introduction of FDA fees for 510(k) reviews—and their recent increase—will motivate companies to take another look at the benefits of third-party review. ■

HOW FAST IS FDA REVIEW?

For a given product category, it is quite easy to find, on-line, typical FDA 510(k) review times. It is necessary to know only the three-letter product code, which can be obtained from FDA on-line databases or from a predicate 510(k).

The entry point to this information is the search panel at www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm. (If typing such a long URL correctly is a challenge, access that search panel from the CDRH Home Page, www.fda.gov/cdrh, click on Databases—under Information Resources—then on Premarket Notifications.) In the search panel, enter the product code and press Search; you will get a list of all 510(k)s cleared under that code, in reverse chronological order of clearance date. Click on a number of these, one at a time, to display details about the most recent clearances. Don't bother looking at devices that you recognize as being very unlike yours (e.g., an accessory versus a complete system). Likewise, eliminate from consideration information on special 510(k)s or those that were reviewed by third parties (all of this information is shown on the details page for each device).

Record the date received and the decision date for about 10 recent submissions and estimate the time that each 510(k) file was open at FDA. Remember that this total time includes any periods where FDA was waiting for additional information that was requested of the sponsor, so it's a good idea to ignore times that seem much longer than most.

From the remaining data, it is possible to get a pretty good idea of how quickly FDA is reviewing 510(k)s for a given product category. Where that time is much longer than a couple of months, third-party review may be particularly appropriate.