

Client Alert

FDA & Life Sciences Practice Group

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FDA Issues New Guidances Regarding Its Preliminary Review of 510(k) Notices and PMA Applications

On December 31, 2012, FDA issued two final guidances that replace prior guidances related to the review of premarket submissions: “Refuse to Accept Policies for 510(k)s” and “Acceptance and Filing Reviews for Premarket Approval Applications (PMAs)” (hereinafter referred to as the 510(k) RTA Guidance and PMA Acceptance and Filing Guidance, respectively). Both guidances went into effect on December 31, 2012 and were issued to help FDA meet its performance goals under the Medical Device User Fee Amendments of 2012 (MDUFA III). We expect FDA to apply the 510(k) RTA and PMA Acceptance and Filing criteria stringently, at least in the near future, resulting in a greater number of submissions not being accepted and/or filed. Therefore, we recommend companies pay close attention to the RTA and Acceptance and Filing criteria and prepare their submissions accordingly.

This client alert highlights key aspects of these guidance documents. Copies of the complete guidance documents are available at <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm162707.htm>.

510(k) RTA Guidance

The 510(k) RTA Guidance is applicable to traditional, special, and abbreviated original 510(k) submissions or responses to RTA communications; it is not applied to supplements or amendments submitted in response to a request for additional information after a 510(k) has been accepted. FDA has 15 calendar days to conduct its preliminary review of a 510(k) notice to determine if it is administratively complete and thus, the Agency can conduct a substantive review of the submission. Under the new 510(k) RTA Guidance, FDA’s review clock does not start until the 510(k) submission has been accepted. The calendar days used to conduct the acceptance review of the accepted submission count toward FDA’s 90-day review period for traditional and abbreviated 510(k) notices and 30-day review period for special 510(k) notices, as well as the 60-calendar goal for Substantive Interaction under MDUFA III.

After confirming payment of the user fee and the submission of an electronic copy (“eCopy”) of the 510(k) notice, FDA will conduct an acceptance review using the checklist for that type of 510(k) notice that is appended to the RTA

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guidance. FDA staff are instructed to answer preliminary questions in traditional and abbreviated 510(k) checklists about whether: (1) the product is a device or a combination product with a device component; (2) CDRH is the appropriate review center; (3) a Request for Designation was submitted for the same device, *i.e.*, that design and indications for us; (4) that type of device is eligible for 510(k) review; (5) a PMA is pending for the same device; and (6) the applicant is under the Application Integrity Policy (AIP) if the 510(k) includes clinical data. The first stage of FDA's acceptance review of a special 510(k) notice is to determine whether the submission meets the following four criteria for that type of submission: (1) the subject device is a modification to a legally marketed (predicate) device for which the submitter is the holder of the cleared 510(k) notice; (2) the device's indications for use have not changed; (3) the device's fundamental scientific technology has not changed; and (4) the submission includes only "summary-level information", *e.g.*, it does not contain performance test reports unless such testing is part of the design validation. If the answers to the preliminary questions show that 510(k) review is appropriate for the traditional or abbreviated submission or the special 510(k) qualifies for that type of review, FDA staff will then complete the rest of that RTA checklist.

Each checklist identifies the elements required in each type of 510(k) notice. The checklists are detailed and seek to reflect the "content needed in traditional, special, and abbreviated 510(k) submissions to allow FDA to conduct a substantive review, thereby enhancing the quality of received 510(k) submissions and improving overall review time." For example, the traditional 510(k) checklist not only requires a test report for each performance test, but also specifies the contents of the report. In addition, the checklist requires that the 510(k) notice include the information identified in a device-specific guidance or needs to demonstrate compliance with a special control for that type of device. The checklist also requires the 510(k) notice to include all of the information that FDA requested or recommended be provided in the submission for the device during the Agency's review of all prior submissions regarding that device, including pre-submissions, investigational device exemption applications, and 510(k) notices that were withdrawn or found not substantially equivalent. The RTA Guidance explains FDA's view that, under its prior RTA policy and checklist, which was less content specific, the Agency "accepted many inadequate submissions for review" and experienced "an inefficient use of resources" in "constructing...extensive letters requesting all of the additional information needed to conduct a substantive review."

If FDA determines that the 510(k) notice contains all the RTA elements, an explanation of any omission or nonconformance, or a statement that any such elements are not applicable, the submission is administratively complete. In that case, FDA will issue an acceptance letter to the applicant and begin the substantive review of the submission. The filing date of the submission will be the date FDA received the document in the Document Control Center (DCC). If the answers to the preliminary questions are not acceptable or FDA determines that the 510(k) notice is not administratively complete, the Agency will refuse to accept the submission. FDA will issue an RTA letter accompanied by the completed acceptance checklist identifying the missing information. If FDA determines that a special 510(k) notice does not meet all of the criteria for that type of review, the Agency will convert the submission to a traditional 510(k) notice and notify the submitter of that action. The guidance document notes that FDA probably will refuse to accept the converted submission because it is unlikely to contain all the RTA elements for a traditional 510(k) notice, *e.g.*, it contains a summary of the performance data rather than the full test report. The applicant then has the opportunity to submit the missing information under the same 510(k) number without paying an additional user fee, and FDA will conduct its acceptance review of the new submission within 15 calendar days of its receipt. If the applicant does not provide the missing information within 180 days of receipt of the RTA letter, the 510(k) will be considered withdrawn and the submission will be closed within FDA's system.

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PMA Acceptance and Filing Guidance

The PMA Acceptance and Filing Guidance applies to all original PMA submissions and panel-track PMA supplements. The new guidance largely follows FDA's previous guidance on PMA filing decisions, but breaks the preliminary review process into two steps--acceptance and filing reviews--rather than a single filing review. FDA's review clock begins only after a PMA submission has been both "Accepted" and "Filed" per the new guidance. FDA's review clock begins as of the date of receipt of the most recent submission or amendment that made the PMA complete and on which the FDA based its acceptance and/or filing decision. It is important to note that this guidance does not alter the statutory criteria under which FDA may refuse to file a PMA (*see* 21 C.F.R. 814.42(e)), the 45-day time period in which a filing decision must be made, or the processes for document distribution/handling and assembling the PMA review team.

Similar to the 510(k) RTA review, the PMA acceptance review is intended to determine whether the PMA application is administratively complete. This review should be conducted within 15 calendar days of receipt of the PMA submission, assuming the user fee has been paid and an eCopy submitted. In determining the acceptability of a PMA submission, FDA staff will answer the same six preliminary questions identified above for traditional and abbreviated 510(k) notices, except the questions about the application type apply to PMAs rather than 510(k) notices. If the preliminary questions show that PMA review is appropriate, FDA staff will determine whether to accept the application by answering the following three decision questions at the end of the acceptance checklist: (1) Is the PMA complete, *i.e.*, does it contain all the required elements listed in that checklist or a rationale for any omission or deviation; (2) Is the PMA supported by information other than isolated case reports, random experiences, reports lacking sufficient details to permit scientific evaluation, and unsubstantiated opinions; and (3) Does the PMA address the key nonclinical and clinical issues that FDA identified prior to the submission of the PMA or a detailed scientific or clinical justification for the alternate approach. If the FDA review team's answer to all of the preliminary questions is that the PMA route is appropriate and its answer to all of those three decision questions is yes, its decision should be to accept the PMA. If the FDA review team's answer to any of those preliminary questions reveals that the PMA route not appropriate or its answer to any of those three decision questions is no, its decision should be to not accept the PMA. If the FDA lead reviewer, branch chief, and division director sign off-on the FDA review team's decision, the Agency will issue a Refuse to Accept letter, accompanied by the completed acceptance checklist indicating which item(s) are the bases for the RTA designation. The applicant then has the opportunity to submit the missing information under the same PMA number and without paying any additional user fee. FDA will conduct its acceptance review of the PMA amendment within 15 calendar days of its receipt. If FDA determines the PMA is administratively complete, the Agency will issue an acceptance letter to the applicant and conduct the filing review.

The intent of the filing review is to determine the adequacy of the technical elements of the PMA and whether the submission is sufficiently complete to allow for a substantive review of the application. The FDA review team answers the following three filing decision questions: (1) Is the data included in the submission consistent with the protocol; (2) Was the clinical study conducted on the final device; and (3) Does the proposed patient/study population match the indications. If the answer to all three questions is yes or the submission contains a scientific or clinical justification for any deviation, the FDA review team's decision should be to file the PMA. If FDA's answer to any of those three question is no and the application does not include a scientific or clinical justification for the deviation, the FDA review team's decision should be to not file the PMA. If the FDA lead reviewer, branch chief, and division director, sign off-on the FDA review team's decision, its decision is final. FDA will notify the applicant in writing

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within 45 calendar days of receipt of the submission whether the PMA has been “Filed” or “Not Filed” (*see* 21 CFR 814.42(a)). If the PMA has been “Filed,” the filing date (*i.e.*, the start of FDA’s review clock) will be the date of receipt of the PMA or of the amendment to the PMA that enabled FDA to file the PMA. If FDA determines that the PMA submission is Not Filed, the Agency will issue a letter detailing the reasons for its decision. The applicant will have the opportunity to submit additional information addressing the identified “not filing” issues under the same PMA number without paying any additional user fee. FDA will then conduct a filing review of the amendment within 45 calendar days of receipt.

Potential Impact

Based on comments made during FDA’s November 27, 2012 webcast on the draft 510(k) RTA and PMA Acceptance and Filing Guidances, the guidances themselves, and our experience with 510(k) notices and PMAs submitted to FDA between issuance of the draft and final guidances, the Agency intends to refuse to file/accept any submission that is not eligible for that type of review and/or does not contain one or more of the required element (or an explanation for any omission or deviation, or a statement that it is not applicable). We strongly recommend that companies carefully review the applicable 510(k) RTA, PMA Acceptance, and PMA Filing checklist(s), any device-specific guidance, any relevant special control document, and communications from FDA about prior submissions regarding the device to determine the required information and include it in the initial submission. We also recommend completing the applicable 510(k) RTA and PMA Acceptance and Filing checklist(s) and including that checklist in that submission. This approach should reduce the risk of refusal, and the resulting delay in the start of the review clock, by ensuring the consistency and completeness of the submission and facilitating FDA’s preliminary review of it.

King & Spalding is happy to assist clients with the preparation and/or review of 510(k) or PMA submissions and to answer questions related to the 510(k) RTA or PMA Acceptance and Filing guidance documents.

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This alert provides a general summary of recent legal developments. It is not intended to be and should not be relied upon as legal advice.