Types of Communication During the Review of Medical Device Submissions

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.
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You should submit comments and suggestions regarding this draft document within **90** days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit written comments to the Division of Dockets Management (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to http://www.regulations.gov. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this document, contact the Premarket Notification (510(k)) Section or the Premarket Approval (PMA) Section of CDRH at 301-796-5640 or CBER's Office of Communication, Outreach and Development at 1-800-835-4709 or 301-827-1800.

When final, this document will supersede "Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs, and BLA Supplements" dated February 28, 2008.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

Preface

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Additional copies of this guidance document are also available from the Center for Biologics Evaluation and Research (CBER), Office of Communication, Outreach and Development (HFM-40), 1401 Rockville Pike, Suite 200N, Rockville, MD 20852-1448, by e-mail at ocod@fda.hhs.gov, or by calling 1-800-835-4709 or 301-827-1800, or from the Internet at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/default.htm.

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Draft Guidance for Industry and Food and Drug Administration Staff

This draft guidance, when finalized, will represent the Food and Drug Administration's (FDA's) current thinking on this topic. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. You can use an alternative approach if the approach satisfies the requirements of the applicable statutes and regulations. If you want to discuss an alternative approach, contact the FDA staff responsible for implementing this guidance. If you cannot identify the appropriate FDA staff, call the appropriate number listed on the title page of this guidance.

1. Introduction

During the review of a premarket submission, FDA's practice has been to communicate with applicants[1] through either a formal communication (such as a Major Deficiency Letter or an additional information request issued through a letter, or through phone, fax, or email, with a follow-up letter confirming the hold) or through the process of Interactive Review. The concept of Interactive Review was discussed in detail in the Commitment Letter from the Secretary of Health and Human Services (the Secretary) to Congress[2] as part of the Medical Device User Fee Act (MDUFA) II of 2007 and the process was further described in the guidance "Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs, and BLA Supplements" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089402.htm).

The Medical Device User Fee Amendments of 2012[3] (MDUFA III), amended the Federal Food, Drug, and Cosmetic Act (FD&C Act) to authorize FDA to collect user fees for the review of certain premarket submissions received on or after October 1, 2012, including premarket notification submissions (510(k)s). The additional funds obtained from user fees will enable FDA, with the cooperation of industry, to improve the device review process to meet certain performance goals and implement improvements for the medical device review process.

[1] An applicant is the same as a holder, sponsor, or submitter for the purposes of this guidance document.
[2] *See* http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/UCM109102.pdf.
[3] See the Food and Drug Administration Safety and Innovation Act of 2012 (FDASIA, Public Law 112-114)

During discussions with representatives of the medical device industry in the development of the Agency's recommendations for MDUFA III,[4] the Agency proposed process improvements to provide further transparency into the review process, including new communication commitments. These additional communications are in the context of: acceptance review;[5] substantive interactions; and, if applicable, missed MDUFA goals. These communications are outlined in the MDUFA III Commitment Letter[6] and are further described in this guidance. In addition, this guidance updates the Agency's approach to Interactive Review to reflect FDA's commitments in the MDUFA III Commitment Letter and to incorporate an expanded use of this communication tool to increase the efficiency of the review process.

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word *should* in Agency guidance documents means that something is suggested or recommended, but not required.

2. Scope

This guidance describes four types of communication that occur during the review of a medical device submission. The four types of communication and the submissions to which they apply are:

- Acceptance Review Communication for premarket notification submissions (510(k)s),[7] original premarket approval applications (Original PMAs), and Panel-Track PMA Supplements;[8,9,10]

[4] Meeting minutes from discussions with the medical device industry on the development of the Agency's recommendations for MDUFA III are available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/MedicalDeviceUserFeeandModernizationActMDUFMA/ucm236902.htm.

[5] FDA has issued guidance on acceptance review: "Refuse to Accept Policy for 510(k)s" available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM315014.pdf and "Acceptance and Filing Review for Premarket Approval Applications (PMAs)" available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313368.pdf.

[6] MDUFA III Commitment Letter, available at http://www.fda.gov/downloads/MedicalDevices/NewsEvents/WorkshopsConferences/UCM295454.pdf (this document is dated April 18, 2012; it has not changed since then).

[7] Acceptance review applies to traditional, special, and abbreviated 510(k) submissions; however, it does not apply to Third Party 510(k)s.

[8] Wherever Original PMAs and Panel-Track PMA Supplements are discussed, the discussion also applies to Premarket Report Applications. These applications are not explicitly referenced in the body of this document given the limited number that FDA receives each year.

[9] Note that as described in the guidance "Acceptance and Filing Review for Premarket Approval Applications (PMAs)," original PMAs and Panel-Track PMA supplements will also undergo a filing review, once accepted, and the outcome of the filing review (i.e., Filed or Not Filed) will be communicated to the applicant. See 21 CFR 814.42.

[10] The MDUFA III Commitment Letter does not include this type of communication for Biologics License Application (BLA) submissions for medical devices. However, BLA submissions for medical devices are subject to

- Substantive Interaction[10] for 510(k)s, Original PMAs, Panel-Track PMA Supplements, and 180-Day PMA Supplements;

- Interactive Review for 510(k)s, Original PMAs, PMA Supplements, original Biologics License Applications (Original BLAs), and BLA Supplements; and

- Missed MDUFA Decision Communication[10] for 510(k)s, Original PMAs, and Panel-Track PMA Supplements.

Appeals (including requests for dispute resolution), pre-submission discussions, and general policy discussions are not within the scope of this guidance document. FDA has issued draft guidance on these topics. See Draft Guidance for Industry and Food and Drug Administration Staff - CDRH Appeals Processes available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm284651.htm; Draft Guidance for Industry and FDA Staff Medical Devices: The Pre-Submission Program and Meetings with FDA Staff available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm310375.htm.

3. Acceptance Review Communication

a. Purpose of Acceptance Review Communication

The purpose of the Acceptance Review Communication is to: (1) identify the lead reviewer or Regulatory Project Manager[11] assigned to the submission and (2) confirm acceptance of the submission or notify the submitter that the submission was not accepted based upon the review of the submission against objective acceptance criteria. FDA has issued guidance documents on acceptance review: "Refuse to Accept Policy for 510(k)s," available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM315014.pdf, and "Acceptance and Filing Review for Premarket Approval Applications (PMAs)," available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313368.pdf.

b. Timing of Acceptance Review Communication

The Acceptance Review Communication should occur within 15 days[12] of receipt of a 510(k), Original PMAs, or a Panel-Track PMA Supplements.

Refuse to File (RTF) criteria and processes; please refer to 21 CFR 601.2(a), "CBER SOPP 8401.3: Filing Action: Communication Options" at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm073085.htm, and "CBER SOPP 8404: Refusal to File Procedures for Biologic License Applications" at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm073474.htm.

[11] All references to lead reviewer in this guidance document are specific to CDRH. For CBER, in all cases, the appropriate contact person is the regulatory project manager (RPM).

[12] For the purposes of this guidance, all "days" refer to calendar days.

c. Content of Acceptance Review Communication

FDA should communicate the outcome of the Acceptance Review to the applicant by fax, email, or other written communication. This communication represents a review of the submission for completeness and is not intended to identify deficiencies that may be identified later in the review cycle.

(1) When the submission is accepted

FDA should provide the name of the FDA lead reviewer or Regulatory Project Manager and notify the applicant that the submission has been accepted. For a 510(k), the submission is accepted for substantive review. For an Original PMA or Panel-Track PMA Supplement, the submission is accepted for filing review.[13]

(2) When the submission is not accepted

FDA should provide the name of the FDA lead reviewer or Regulatory Project Manager and notify the applicant that the submission has not been accepted and identify those items necessary for the submission to be considered accepted.

4. Substantive Interaction

a. Purpose of Substantive Interaction

The purpose of Substantive Interaction is to communicate to the applicant one of the following:

- FDA intends to continue working with the applicant to resolve any outstanding deficiencies via Interactive Review, and the submission will not be placed on hold; or
- FDA has identified deficiencies that warrant placing the submission on hold.

An approval, approvable, or clearance letter issued prior to the Substantive Interaction goal date is considered an on-time Substantive Interaction for the purpose of meeting the MDUFA III goal.

b. Timing of Substantive Interaction

Substantive Interaction should occur following acceptance of the submission and after FDA has performed a complete review[14] of the submission and within:

- 60 days of the receipt date of a complete submission for 510(k)s;

[13] For those PMA submissions that are accepted for filing review, FDA will communicate the filing status within 45 calendar days of receipt of a complete application. See 21 CFR 814.42. For those applications that are not filed, FDA intends to communicate the specific reasons for rejection and the information necessary for filing. See the guidance document entitled "Acceptance and Filing Reviews for Premarket Approval Applications," available at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313368.pdf.

[14] In some cases, a complete review for a 510(k) may not be warranted because FDA has determined that there is a new intended use or technological difference that raises a new question of safety and effectiveness.

- 90 days of the filing date for Original PMAs and Panel-Track PMA Supplements; and
- 90 days of the receipt date for 180-Day PMA Supplements.

c. Content of Substantive Interaction

Based on the nature and/or extent of the deficiencies, the submission may or may not be placed on hold.

(1) When the submission is not placed on hold

FDA should inform the applicant that the agency does not intend to place the submission on hold and that any additional deficiencies will be handled through Interactive Review. The tools for this communication include the same as those used for Interactive Review (see Section 5d below). Regardless of which communication tool is used, FDA is ultimately responsible for ensuring a complete administrative file for each submission. This type of Substantive Interaction has no start/stop impact on the review clock.

(2) When the submission is placed on hold

FDA intends to place the submission on hold in accordance with current practice.[15, 16] Deficiencies identified in the hold request should be based upon a complete review of the entire submission, and should include both major and any unresolved minor deficiencies.[17]

5. Interactive Review

a. Purpose of Interactive Review

The purpose of the Interactive Review process is to facilitate the efficient and timely review and evaluation by FDA of premarket submissions through increased informal interaction between FDA and applicants, including the exchange of scientific and regulatory information. More specifically, the Interactive Review process is designed to help accomplish the following:

- improve the interaction between the FDA review staff and the applicant during the review process;

[15] For information regarding the effect of agency and industry actions pertaining to premarket review of 510(k)s on the FDA review clock and MDUFA goals, refer to the guidance document entitled, "FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Goals," available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089735.htm).

[16] For information regarding the effect of agency and industry actions pertaining to premarket review of PMAs on the FDA review clock and MDUFA goals, refer to the guidance document entitled, "FDA and Industry Actions on Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Performance Assessment," available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089733.htm.

[17] For PMAs, the hold letter may not include all minor deficiencies associated with labeling and post-approval studies as these items cannot typically be fully reviewed until the major deficiencies have been successfully addressed.

- prevent unnecessary delays in the completion of the review, thus reducing the overall time to market;
- ensure that FDA's concerns are clearly communicated to the applicant during the review process, as appropriate;
- minimize the number of review cycles;
- minimize the number of review questions conveyed through deficiency letters; and
- ensure timely responses from applicants.

Interactive Review has no start/stop impact on the review clock.

b. Types of Deficiencies Appropriate for Interactive Review

FDA has found that Interactive Review can be used more broadly than suggested by the guidance, "Interactive Review for Medical Device Submissions: 510(k)s, Original PMAs, PMA Supplements, Original BLAs, and BLA Supplements." This initial guidance indicated that only minor deficiencies (e.g., those deficiencies that, if unaddressed, could be communicated in a PMA approvable letter) would be considered appropriate for Interactive Review. However, FDA has found that the benefits of Interactive Review could be expanded by using Interactive Review to address deficiencies that are more significant than "minor," but that can likely be addressed by the applicant in a time frame that would allow FDA review of the response prior to the MDUFA performance goal for that submission type[18] without placing the submission on hold. Examples include, but are not limited to: requests for limited additional short-term laboratory bench or biocompatibility testing; further justification for the omission of a test; and additional statistical analysis of the clinical data not related to the primary safety or effectiveness endpoint. FDA review staff should obtain appropriate management input and approval prior to communication of any deficiencies.

c. Timing of Interactive Review

(1) Interactive Review After Substantive Interaction for 510(k)s, Original PMAs, Panel-Track PMA Supplements, and 180-Day PMA Supplements

Following a Substantive Interaction that places the submission on hold, the submission will not be considered under review until receipt of a complete response, in which the applicant provides the requested information, an alternative means of addressing each cited deficiency, or a justification for why the requested information was not necessary. After receipt of a complete response, FDA should interact with the applicant to resolve any remaining deficiencies that might reasonably be addressed through Interactive

[18] Performance goals for each submission type are addressed in the guidance documents, "FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Goals." (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089735.htm) and "FDA and Industry Actions on Premarket Approval Applications (PMAs): Effect on FDA Review Clock and Goals" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089733.htm).

Review. Any new deficiencies (i.e., deficiencies not raised as part of the Substantive Interaction) should be limited to issues raised by the information provided by the applicant in its response, unless the reviewer concludes (and received supervisory concurrence) that the initial deficiencies identified do not adequately address important issues materially relevant to a decision of substantial equivalence (510(k)) or safety and effectiveness (PMA).[19] For example, following the communication of deficiencies in a 510(k) AI letter, FDA might become aware of a heightened potential for device failure through a series of recalls on other devices with a similar feature. If these recalls indicate that the particular bench test performed by the applicant to evaluate this feature is not predictive of clinical performance, an FDA reviewer, with appropriate supervisory concurrence, might request additional testing to address the safety of this feature to determine substantial equivalence. As the end of the review cycle approaches, FDA intends to send a communication that lists the remaining issues, limiting the applicant's response timeframe to a maximum of 7 calendar days and allowing time for FDA to review the response, so that a timely MDUFA decision can be made.

However, if the outstanding deficiencies following the applicant's response to the Substantive Interaction include issues that are not likely to be resolved through Interactive Review (e.g., a device submitted in a 510(k) has a new intended use or different technological characteristics that raise new questions of safety or effectiveness; a new clinical study will be needed for a device submitted in a PMA), FDA may proceed with issuing a Not Substantially Equivalent (NSE) letter for a 510(k) or a Not Approvable (NOAP) letter for a PMA without engaging in Interactive Review.

In limited circumstances, a second AI letter for a 510(k) may be appropriate. One example of such a circumstance would be when a first AI letter indicates that FDA believes no predicate device exists, but the submitter is able to identify a predicate. A subsequent review of the comparison of the subject device to the newly identified predicate could raise questions appropriate for a second AI request. Other instances in which a second AI request could be issued should be limited and occur only with concurrence of Division-level management.

Occasionally applicants ask FDA to issue a second letter (either AI or Major Deficiency) to place the submission on hold to facilitate the completion of performance testing to address one or more deficiencies outstanding following the response to the Substantive Interaction. FDA believes that where the applicant should know what data are needed for its device to meet the applicable review standards (e.g., because of guidance, web-posted 510(k) summaries, or PMA Summaries of Safety and Effectiveness Data), the initial submission should be complete, and, therefore, a second hold letter would be contrary to the stated goal of MDUFA III to reduce the number of review cycles and the Total Time

[19] For more information on requests for additional information pertaining to subsequent interactions, refer to the CDRH SOP entitled, "SOP: Decision Authority for Additional or Changed Data Needs for Premarket Submissions," available at http://www.fda.gov/AboutFDA/CentersOffices/OfficeofMedicalProductsandTobacco/CDRH/CDRHReports/ucm279288.htm.

to Decision.[20] Where it is not reasonably known what data are necessary for a device (e.g., guidance is not clear or the device incorporates a new technology or feature), the agency refers the applicant to the Pre-Submission Program[21] to obtain FDA's recommendations for the planned submission.

(2) Additional Interactive Review

While section c.(1) (above) describes how Interactive Review is expected to occur after Substantive Interaction, FDA also encourages the use of Interactive Review at other points in the review process to facilitate the efficient and timely review of a submission. At FDA's discretion, Interactive Review can be used:

- prior to Substantive Interaction for 510(k)s, Original PMAs, Panel-Track PMA Supplements, and 180-Day PMA Supplements; and

- as needed for BLAs, BLA supplements, Humanitarian Device Exemptions (HDEs), and Product Development Protocols (PDPs).

FDA should determine an acceptable timeframe for the applicant to provide a response to the deficiencies based on MDUFA, Office, or Center timelines. The established timeframe should be based on the impending review deadline, the estimated time that the applicant should need to respond, and the estimated time that FDA should need to review the response.

d. Communication Tools for Interactive Review

Communication tools that should facilitate Interactive Review are described below. Application of these communication tools should remain flexible to balance speed and efficiency with the need to ensure appropriate FDA supervisory concurrence. Appropriate communication tools for Interactive Review include the following:[22]

- Email and Fax[23] - FDA's preferred mechanisms for communication are email and fax because they are efficient and create a permanent record of the interaction.

[20] The term "Total Time to Decision" is defined in the MDUFA III Commitment Letter, See footnote 6.

[21] FDA has issued draft guidance on Pre-Submissions, entitled, "The Pre-Submission Program and Meetings with FDA Staff" available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm310375.htm. Once final, this document will represent the FDA's thinking on this topic.

[22] FDA does not intend to issue letters as part of the Interactive Review process and, accordingly, information regarding letters was removed from the Interactive Review section of this updated guidance.

[23] See the following CBER Standard Operating Procedures and Policies for more information: "SOPP 8113: Handling of Regulatory Faxes" available at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm079472.htm and "SOPP 8119: Use of Email for Regulatory Communications" available at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm109645.htm.

All email communications, including during interactive review, between industry and FDA (in both directions) are unencrypted (not secure) unless regulated firms and/or their representatives have taken steps to create a secure email communication channel with the Agency. Some companies in the medical device industry have already taken the steps necessary to establish secure email communications, but many others have not. Please note that secure email is the preferred option for CBER. Companies wishing to establish secure email communications with FDA should send an email to SecureEmail@fda.hhs.gov. The Agency's Office of Information Management will contact the sender to let them know what they need to do, or what they need to pass on to their IT support person/group to establish this secure communications link.

- Phone Calls[24,25] - Phone calls should be used primarily for requests for clarification that the FDA reviewer can easily document (e.g., the location of specific information within the submission, interpretation of a graph).

- Submission Issue Meetings (face-to-face meetings, teleconferences/videoconferences)[26] - Meetings are important tools for interacting on a submission. However, because meetings involve coordinating the availability of multiple FDA staff and company representatives, they typically involve additional planning and administrative efforts. Therefore, FDA and the applicant should consider whether a meeting is the most appropriate and effective communication mechanism to resolve the issue(s) while the submission is under review.[27]

Regardless of which communication tool is used, FDA is ultimately responsible for ensuring a complete administrative file or each submission.

e. Responses to Deficiencies Requested via the Interactive Review Process

FDA should accept email responses to the information requested via the Interactive Review process and include that information as part of the official administrative file for the submission. FDA should not request that the applicant also formally submit these Interactive Review responses to the appropriate Document Control Center (DCC) as part of an official submission.

Please note that eCopy requirements do not apply to information obtained during the Interactive Review process (via email, phone, and/or fax) once a submission is under

[24] See the following CBER Standard Operating Procedures and Policies for more information: "SOPP 8104: Documentation of Telephone Contacts with Regulated Industry" available at http://www.fda.gov/BiologicsBloodVaccines/GuidanceComplianceRegulatoryInformation/ProceduresSOPPs/ucm079463.htm.

[25] CDRH staff should include documentation of the teleconference (including the names of the participants, date and time held, and substantive issues discussed) through an email to the document management system.

[26] FDA has issued draft guidance on Submission Issue Meetings, entitled "The Pre-Submission Program and Meetings with FDA Staff" available at http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm310375.htm. Once final, this document will represent the Agency's current thinking on this topic.

[27] Applicants should not request meetings for the purpose of obtaining a pre-assessment of the adequacy of data already submitted or to be submitted.

review, if that information is not submitted to CDRH's or CBER's DCC. However, should an applicant choose to submit a response to an Interactive Review request to CDRH's or CBER's DCC (which should only occur if the size of the response makes communication by email or fax infeasible), it will be logged in as an amendment and be subject to the eCopy requirements.[28]

f. Applicant's Role in the Interactive Review Process

(1) What the Applicant Can Do to Help Ensure an Efficient Interactive Review Process

To help ensure that the Interactive Review process is effective, the applicant should do the following:

- submit a well organized and administratively and scientifically complete submission consistent with applicable regulations, recommendations in the available guidance documents, and communications with FDA prior to submission;

- provide complete contact information in the cover letter (i.e., name, email, phone number, fax number) accompanying each formal submission. FDA also recommends providing alternative contact information in case the lead contact is not available. In addition, foreign applicants should have a U.S. representative[29] available to participate in the Interactive Review process and to provide a means to contact the foreign company as quickly as possible;

- apply appropriate material or testing standard(s) and submit the necessary declarations or data to support the use of the standard(s); and

- provide a complete response to all deficiencies communicated via Interactive Review within the FDA-allotted timeframe

(2) Examples of When the Applicant Should Contact the Lead Reviewer or Regulatory Project Manager

Examples of when the applicant should contact the lead reviewer of the submission include the following:[30]

- to reconcile any disagreement with a deficiency cited by the lead reviewer or consulting reviewer during Interactive Review;

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[28] For more information about the eCopy program, see the guidance, "eCopy Program for Medical Device Submissions," at http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM313794.pdf.

[29] If a PMA applicant does not reside or have a place of business within the U.S., the PMA must be countersigned by an authorized representative residing or maintaining a place of business in the U.S. and must identify the representative's name and address (21 CFR 814.20(a)). Identification of and contact information for a U.S. agent is required for all foreign device manufacturers when they register and list with FDA (21 CFR 607.40(d) and 21 CFR 807.40(b)). To facilitate timely communication, it is recommended that a U.S. representative be included for all submission types, in addition to PMAs.

[30] The examples are specific to the Interactive Review process when the submission is under review.

- to inquire whether a revised Interactive Review timeframe may be given to address a deficiency because the initial timeframe cannot be met;
- to discuss procedural questions related to the submission;
- to correct errors in the data submitted;
- to clarify information in the submission that the applicant subsequently notices is unclear; and
- to alert FDA that it intends to submit new, unsolicited information or data (depending on its extent, the information/data may necessitate a new 510(k) or be logged in as an unsolicited major amendment for a PMA, PMA Supplement, BLA, or BLA Supplement).

Applicants should refrain from using Interactive Review to request status updates as such requests may interfere with FDA's ability to meet applicable timeframes.

g. FDA Review Team Considerations

FDA consulting reviewers, like the lead reviewer, should participate in the Interactive Review of submissions. However, the lead reviewer should determine whether or not a consulting reviewer should communicate directly with the applicant or communicate to the applicant through the lead reviewer to resolve minor deficiencies.

In cases where a consulting reviewer communicates directly with the applicant on a particular deficiency, a documented record of the exchange should be made available to the lead reviewer (e.g., "cc" on an email). The consulting reviewer is also expected to document any interaction as part of his/her review record back to the lead reviewer.

6. Missed MDUFA Decision Communication

a. Purpose of Missed MDUFA Decision Communication

The purpose of this communication is to facilitate a timely resolution to any outstanding issues that have precluded FDA from reaching a MDUFA decision prior to the appropriate MDUFA decision goal.

b. Timing of Missed MDUFA Decision Communication

A Missed MDUFA Decision communication should occur for those submissions that have not reached a MDUFA decision by:

- 100 FDA days for 510(k)s; and
- 20 FDA days after the applicable FDA day goal for Original PMAs and Panel-Track PMA Supplements.

c. Content of Missed MDUFA Decision Communication

FDA intends to provide written (e.g., email) feedback to be discussed in a meeting or teleconference. The feedback should reflect appropriate management input and approval and should include:

- all outstanding issues with the application preventing FDA from reaching a decision;[31]
- action items for FDA and/or the applicant;
- the estimated completion date for the action items identified for each party; and
- proposed dates for meetings from which the applicant may choose (the applicant may, in turn, propose alternative dates to FDA).

Outstanding issues should be resolved through Interactive Review whenever possible. If all of the outstanding issues are adequately presented through the written correspondence, FDA and the applicant can agree that a meeting or teleconference is not necessary.

[31] Note that "issues" in this context refers to the major outstanding review topic areas or other reasons that are preventing FDA from reaching a MDUFA decision and not necessarily to individual deficiencies. Any specific outstanding deficiencies that preclude approval should not be included in this communication, but should be communicated informally through Interactive Review or formally in a MDUFA decision letter.