510(k) Third Party Review Program and Third Party Emergency Use Authorization (EUA) Review

Draft Guidance for Industry, Food and Drug Administration Staff, and Third Party Review Organizations

DRAFT GUIDANCE

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Document issued on December 21, 2023.

You should submit comments and suggestions regarding this draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852-1740. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

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When final, this guidance will supersede "510(k) Third Party Review Program; Guidance for Industry, Food and Drug Administration Staff, and Third Party Review Organizations" issued on March 12, 2020.

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Preface

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This draft guidance, when finalized, will represent the current thinking of the Food and Drug Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff or Office responsible for this guidance as listed on the title page.

I. Introduction

The 510(k) Third Party (3P510k) Review Program (formally known as the Accredited Persons (AP) Program) is authorized under section 523 of the Federal Food, Drug, and Cosmetic Act (FD&C Act).[1] Under the authority in section 523 of the FD&C Act, FDA recognizes third parties to review premarket notification ("510(k)") submissions and recommend the initial classification of certain devices.[2] FDA's implementation of section 523 of the FD&C Act establishes a process

[1] Section 523 of the FD&C Act uses the terms "accredited persons," "accredit," "accredited," "accreditation," "reaccredit," "reaccredited," and "reaccreditation." The guidance does not use those statutory terms but rather defines such terms as "recognition," and "rerecognition" as synonymous terms. These alternative terms are used in this guidance to harmonize the terms used by FDA and in the FD&C Act with those in the International Medical Device Regulators Forum (IMDRF) Good Regulatory Review Practices (GRRP) documents and are defined in Section IV of this guidance.

[2] Section 201(h)(1) of the FD&C Act provides that the term "device" is defined as follows:

"an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including any component, part, or accessory, which is--

(A) recognized in the official National Formulary, or the United States Pharmacopeia, or any supplement to them,

(B) intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or

for recognition of qualified third parties to conduct the initial review of 510(k) submissions for certain low-to-moderate risk devices eligible for review under the 3P510k Review Program within the Center for Devices and Radiological Health (CDRH) that are submitted directly to a 3P510k Review Organization (3P510k RO).[3]

FDA may contract with third party review organizations to perform reviews of Emergency Use Authorization (EUA) requests (3PEUA review) when appropriate emergency declaration authorities are active under section 564 of the FD&C Act. FDA has previously contracted with third party review organizations to perform reviews for 3PEUA review when appropriate emergency declaration authorities are active under section 564 of the FD&C Act.

For the current edition of the FDA-recognized standards referenced in this document, see the FDA Recognized Consensus Standards Database.[4] For more information regarding use of consensus standards in regulatory submissions, please refer to the guidance "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices."[5]

The objectives of this guidance are:

- To describe and distinguish FDA's expectations for the 3P510k Review Program and for 3PEUA review;
- To describe the factors FDA will use in determining device type eligibility for review by 3P510k ROs;
- To outline FDA's process for the recognition, rerecognition, suspension, and withdrawal of recognition for 3P510k ROs;
- To clarify FDA's expectations for review under both 3P510k review and 3PEUA review for all stakeholders to ensure confidence and consistent quality of work by Third Party Review Organizations[6] to eliminate the need for routine, substantive re-review by FDA;[7]
- To outline FDA's expectations to prevent conflicts of interest between the Third Party Review Organization(s) and other entities; and
- To describe FDA's expectations regarding the compensation process between the Third Party Review Organization(s) and other entities.

(C) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of its primary intended purposes. The term 'device' does not include software functions excluded pursuant to section 520(o)" of the FD&C Act.

[3] Devices of the types eligible for 3P510(k) review are not currently being reviewed in the Center for Biologics Evaluation and Research.

[4] Available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

[5] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices

[6] As described in Section IV of this guidance, the use of "Third Party Review Organizations" indicates an expectation for both 3P510k and 3PEUA ROs.

[7] See "Eliminating Routine FDA Re-Review of Third Party 510(k) Reviews," available at https://www.fda.gov/media/116168/download

In general, FDA's guidance documents 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 guidances means that something is suggested or recommended, but not required.

II. Background

A. Basis for 3P510k Review Program

On August 1, 1996, FDA launched a voluntary third party 510(k) review pilot program for selected medical devices. Under this pilot program, all class I devices that were not 510(k) exempt at that time, and 30 class II devices were eligible for 3P510k review.

On November 21, 1997, the Food and Drug Administration Modernization Act (FDAMA)[8] was signed into law. Section 210 of FDAMA codified and expanded the pilot program by establishing section 523 of the FD&C Act.

On July 9, 2012, the Food and Drug Administration Safety and Innovation Act (FDASIA)[9] was signed into law and required FDA to establish and publish criteria to accredit, reaccredit, and deny reaccreditation of 3P510k ROs that perform 510(k) reviews of eligible devices.

On August 18, 2017, the FDA Reauthorization Act of 2017 (FDARA)[10] was signed into law and required FDA to issue guidance on the factors FDA will use in determining whether a class I or class II device type, or subset of such device types, is eligible for review by 3P510k ROs, including the risk of the device type and whether the device type is permanently implantable, life sustaining, or life supporting, and whether there is a detailed public health justification for permitting the review by an accredited person of such device type. This guidance also addresses several Medical Device User Fee Amendments (MDUFA) IV[11] and V[12] commitments by including an early interaction (EI) consult policy; clarifying criteria for rerecognition of 3P510k ROs and the suspension or withdrawal of recognition; encouraging thorough review memoranda to reduce the need for FDA re-review; and discussing how FDA will audit the 3P510k Review Program as part of ongoing audit plans under the Quality Management and Organizational Excellence (QMOE) Program.

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[8] Pub. L. 105-115.

[9] Pub. L. 112-144.

[10] Pub. L. 115-52.

[11] Through the MDUFA IV Commitment Letter, FDA commits to improving the Third Party Review Program with a goal of eliminating routine re-review by FDA of 3P510k reviews: See 163 CONG. REC. S4729-S4736 (daily ed. August 2, 2017) (Food and Drug Administration User Fee Reauthorization), also available at https://www.fda.gov/media/102699/download

[12] As described in Section V.D. of the MDUFA V Commitment Letter, FDA will continue to support the Third Party Review program, with the objective of eliminating routine re-review by FDA of Third Party reviews: See 168 CONG. REC. S5195-S5200 (daily ed. September 28, 2022) (Food and Drug Administration User Fee Reauthorization), also available at https://www.fda.gov/media/158308/download

B. Basis for Third Party EUA Review

In 2019, an outbreak of respiratory disease caused by a novel coronavirus began. The virus has been named "SARS-CoV-2," and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19). The COVID-19 pandemic presented FDA with an unprecedented workload across many device areas, including and perhaps especially, in vitro diagnostics to detect SARS-CoV-2. In response to the COVID-19 pandemic, an unprecedented number of manufacturers came forward to request EUAs for in vitro diagnostic products for detection of SARS-CoV-2. The manufacturers included those familiar and unfamiliar with FDA regulation. As scientific understanding advanced, FDA was able to offer templates to developers outlining FDA's expectations for the development of prescription tests for SARS-CoV-2 across different technologies, including molecular, antigen, and serology tests. As the number of tests that were issued EUAs related to COVID-19 grew to meet demand, FDA focused on reviewing EUA requests for tests with new intended uses, such as over-the-counter tests for home use. At the same time, FDA continued to receive a large volume of EUA requests for tests with intended uses and technologies with which FDA had performed sufficient reviews such that it generally understood the information needed to support such an EUA request. Consequently, FDA contracted with a 3PEUA Review Organization (3PEUA RO) to review and provide recommendations on over one hundred in vitro diagnostic device EUA requests.

On December 29, 2022, the Prepare for and Respond to Existing Viruses, Emerging New Threats, and Pandemics Act (PREVENT Pandemics Act) was signed into law as part of the Consolidated Appropriations Act, 2023 (hereafter referred to as the "FY 2023 Omnibus").[13] Section 2502 of the FY 2023 Omnibus amends section 565 of the FD&C Act to add subsection (i), which clarifies FDA's authority regarding use of third party review organizations to conduct initial reviews of EUA requests for in vitro diagnostic products. It further directs FDA to issue guidance on such third party review, including considerations on compensation, information sharing, and conflicts of interest. This guidance update is intended to satisfy FDA's obligation to issue draft guidance on consultations with persons under section 565(i) of the FD&C Act and to provide clarity on use of 3PEUA review for devices other than in vitro diagnostic products. When final, it will provide FDA's current thinking on 3PEUA review.

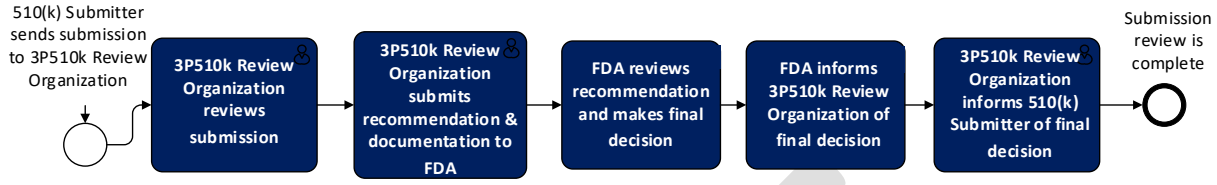
C. General Overview of 3P510k Review Program

The 3P510k Review Program is intended to support FDA's mission to protect and promote public health by enabling the Agency to focus its internal scientific review resources on higher-risk and complex devices, while maintaining a high degree of confidence in the review of low-to-moderate risk and less complex devices by 3P510k ROs, and to provide manufacturers of

[13] See Pub. L. No. 117-328, available at https://www.congress.gov/bill/117th-congress/senate-bill/3799/text#toc-id4337B43372204E669A25EB3B18C8F11F

eligible devices a voluntary alternative review process that may yield more rapid decisions on 510(k)s.[14] Figure 1 below provides a schematic overview of the 3P510k Review Program.[15]

Figure 1 – A General Overview of the 3P510k Review Program



Under the 3P510k Review Program, 3P510k ROs review a 510(k) submission and then forward their review, the 510(k) submission, and a recommendation to FDA (i.e., substantially equivalent (SE) or not substantially equivalent (NSE) as defined under section 513(i) of the FD&C Act) as described in more detail in Section VI.B.(6) of this guidance. FDA reviews the 3P510k RO's memo and recommendation and makes a final decision on the submission. Section 523(a)(2) of the FD&C Act requires FDA to make a determination with respect to the initial classification within 30 calendar days[16] after receiving a recommendation from a 3P510k RO. In this pathway, the 510(k) Submitter pays the 3P510k RO directly; no user fee is due to FDA for the 510(k) reviewed by the 3P510k RO.[17] A general principle of the 3P510k Review Program is that the 3P510k RO is the conduit for communication to and from the 510(k) Submitter and to and from the FDA. This ensures the 3P510k RO is fully informed and that communications between FDA and the 510(k) submitter do not undermine the role of the 3P510k RO.

A 3P510k RO must be recognized by FDA under section 523(b) of the FD&C Act to be eligible to participate in the 3P510k Review Program. FDA recognizes 3P510k ROs[18] to review 510(k)s for certain device types eligible for the 3P510k Review Program.[19]

Participation by 510(k) Submitters in the 3P510k Review Program is voluntary. Manufacturers who do not wish to use a 3P510k RO may submit their 510(k)s directly to the FDA for review,

[14] See section 523(a)(3) of the FD&C Act.
[15] Figure 1 uses IEC/IEC 19510: Information technology – Object Management Group Business Process Model and Notation (2013).
[16] FDA uses calendar days when measuring on-time performance of user-fee supported premarket medical device submission reviews. For more information, see "MDUFA Performance Goals and Procedures, Fiscal Years 2023 through 2027," available at https://www.fda.gov/media/158308/download
[17] See section 738(a)(2)(B)(iv) of the FD&C Act.
[18] A current list of recognized 3P510k ROs is available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfThirdParty/Accredit.cfm
[19] A current list of eligible devices for review under the 3P510k Review Program is available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfThirdParty/current.cfm

through either the Traditional, Special, or Abbreviated Programs, as appropriate, and pay the appropriate FDA user fee.[20, 21, 22]

As described in this guidance, the 3P510k Review Program includes features designed to ensure a high level of quality in the review of 510(k)s by a 3P510k RO and to minimize risks to public health. In evaluating a 3P510k RO for recognition or rerecognition, FDA will consider not only the application, as outlined in Section V.D of this guidance, but may also consider past premarket review performance of the 3P510k RO as described in Section V.D.(2) of this guidance.[23]

D. General Overview of 3PEUA Review

3PEUA review is intended to support FDA's mission to protect and promote public health by enabling the Agency to "surge" or rapidly expand its resources for reviewing EUA requests relating to medical devices. Under section 564 of the FD&C Act, FDA may, after the Secretary of Health and Human Services (HHS) has made a declaration of emergency or threat justifying authorization of emergency use (an "EUA declaration"), authorize the emergency use of an unapproved product[24] or an unapproved use of an approved product for certain emergency circumstances. FDA may issue an EUA to allow a product to be used to diagnose, treat, or prevent a serious or life-threatening disease or condition referenced in the EUA declaration, when certain statutory criteria are met, including FDA's determination under section 564(c)(2) of the FD&C Act that, based on the totality of scientific evidence, the product may be effective for such use, the known and potential benefits outweigh the known and potential risks for such use, and, under section 564(c)(3) of the FD&C Act, that there are no adequate, approved, and available alternatives.[25]

To assist FDA in reviewing EUA requests in a timely manner, FDA may establish a contractual relationship with one or more qualified 3PEUA ROs to conduct such reviews. In general, FDA intends for EUA requests to be submitted directly to FDA. and FDA may, at our discretion, then

[20] See the guidance "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k

[21] See the guidance "The Abbreviated 510(k) Program," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/abbreviated-510k-program

[22] See the guidance "The Special 510(k) Program," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/special-510k-program

[23] See sections 523(b)(2) and 523(b)(3) of the FD&C Act.

[24] For purposes of this document, the term 'unapproved product' refers to a product that is not approved, licensed, or cleared under section 505, 510(k), 513 or 515 of the FD&C Act; an 'unapproved use of an approved product' refers to a product that is approved, licensed, or cleared under such a provision but for which the specific use is not an approved, licensed, or cleared use of the product. See 'unapproved product' and 'unapproved use of an approved product' in section 564(a)(2) of the FD&C Act.

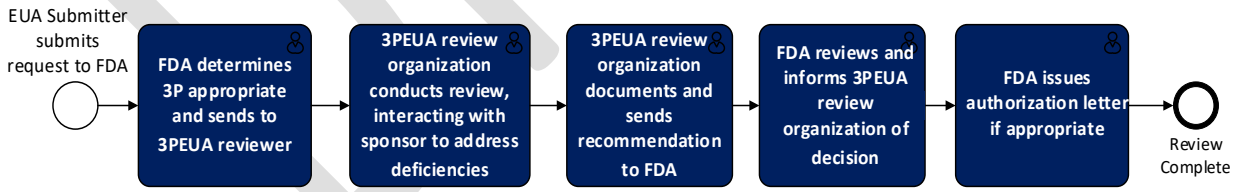
[25] For more information on FDA's emergency use authorities under section 564 of the FD&C Act, see the guidance "Emergency Use Authorization of Medical Products and Related Authorities," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities

forward the EUA request to 3PEUA ROs, as appropriate.[26] The 3PEUA RO should work with the submitter to address any deficiencies identified by the 3PEUA RO, document its review, and forward its recommendation to FDA in writing. FDA will conduct the final review and may issue an EUA, as appropriate. More specifically, FDA will consider recommendations from 3PEUA ROs related to whether the standard under section 564(c)(2) of the FD&C Act is met, as well as recommendations pertaining to the scope of authorization under section 564(d) of the FD&C Act and conditions of authorization under section 564(e) of the FD&C Act. FDA does not intend to consider recommendations from 3PEUA ROs relating to other criteria for issuance of an EUA, such as whether there are adequate, approved, and available alternatives. Typically, FDA will likely have more information on these issues than the 3PEUA RO. Figure 2 below provides an overview of 3PEUA review.[27]

Accurate and reliable diagnostic tests are critical to the tracking, treatment, and suppression of transmission during an emergency. In order to respond quickly and increase access in certain emergency situations, for in vitro diagnostic products,[28] FDA may determine that public health would be better served by having submitters send certain EUA requests for in vitro diagnostic products directly to a 3PEUA RO. In such case, FDA plans to include information on the public website regarding submission of EUA requests directly to specified 3PEUA ROs. Relevant in vitro diagnostic product codes and other device specifics (e.g., specimen type, use setting) will also be listed on that website.[29] The same review process is intended to apply for EUA requests sent directly to a 3PEUA RO.

Note that for review of EUA requests, FDA may contract with 3PEUA ROs when appropriate emergency declaration authorities are active under section 564 of the FD&C Act. Given that the needs of an EUA declaration and the scientific expertise appropriate to reviewing EUA submissions will typically not be known prior to an emergency, FDA does not anticipate identifying potential 3PEUA ROs in advance. The terms of a contract between FDA and a 3PEUA RO will control over this guidance.

Figure 2 – A General Overview of 3PEUA Review



[26] FDA generally intends to contract with 3PEUA ROs when there are, or are anticipated to be, a large volume of EUA requests or certain types of EUA requests and, based on the circumstances of an emergency, the Agency determines that help with review would be beneficial.

[27] Figure 2 uses IEC/IEC 19510: Information technology – Object Management Group Business Process Model and Notation (2013).

[28] See 21 CFR 809.3.

[29] For a list of relevant devices for 3PEUA review, please visit FDA's website at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfThirdParty/current.cfm

3PEUA review differs from the 3P510k Review Program in several ways. Some of the main differences are:

- 3PEUA review may only occur following a relevant declaration under section 564 of the FD&C Act justifying emergency use authorization of a product. Assignment of a EUA request will be determined at FDA's discretion.
- EUA Submitters should send EUA requests directly to FDA, and FDA may decide to send certain EUA requests to a 3PEUA RO for review. For in vitro diagnostic products, FDA may determine that the public health would be better served by having submitters send EUA requests directly to a 3PEUA RO.
- FDA may contract with 3PEUA ROs directly. This includes the review of EUA requests for in vitro diagnostic products where FDA determines it would be appropriate to send EUA requests directly to a 3PEUA RO.

Section V of this guidance clarifies FDA's expectations for the 3P510k Review Program and for 3PEUA review, as applicable. As noted in Section IV of this guidance, references to "Third Party Review Organization" indicate an expectation for both 3P510k ROs and 3PEUA ROs.

III. Scope

This guidance outlines FDA's current thinking on key aspects of the 3P510k Review Program and 3PEUA review, including:

- Factors used to establish device type eligibility in the 3P510k Review Program (see Section V.A);
- FDA's expectations for third party reviews of 510(k) and EUA submissions, including the policy for EI consults on 3P510k submissions (see Section V.B);
- Requirements and considerations for recognition and rerecognition of 3P510k ROs under the 3P510k Review Program (see Section V.C);
- Content and format of a 3P510k RO's application for initial recognition and rerecognition (see Section V.D);
- Process for suspension or withdrawal of recognition for 3P510k ROs (see Section V.E); and
- Leveraging the International Medical Device Regulators Forum's (IMDRF's) requirements for Regulatory Reviewers under the Good Regulatory Review Practices (GRRP), as appropriate (see Section V.F).

IV. Definitions

The definitions provided below explain the terms used by FDA in the context of this guidance. These terms are not intended to be applied in any context beyond this document, the 3P510k Review Program, and 3PEUA review.

Device Type: A device type or category as set forth in a section of the Code of Federal Regulations, as well as a subset of such device type, such as that set forth in a product code.

EUA Submitter: An entity or person that submits a request for Emergency Use Authorization under section 564 of the FD&C Act.

510(k) Submitter: An entity or person that submits a 510(k) submission to a 3P510k Review Organization for the purposes of demonstrating substantial equivalence (SE) of that device to a legally marketed device that is not subject to premarket approval (PMA).

Final Reviewer: An individual within the Third Party Review Organization who oversees the review of a 510(k) submission or EUA request throughout the entire review process. The Final Reviewer is a regulatory reviewer who meets the criteria of an IMDRF Regulatory Reviewer (defined below) and who is responsible for ensuring that final recommendations regarding the device made by the Product Specialist (defined separately) are appropriately evaluated, organized, and documented before documents are sent to FDA. This individual has sufficient authority and competence within the Third Party Review Organization to independently evaluate the quality and acceptability of the Third Party review documentation. The Final Reviewer is a separate individual from the Product Specialist.

IMDRF Regulatory Reviewer: An individual meeting and fulfilling the competencies, commitments, training, and conduct described in IMDRF/GRRP WG/N40 FINAL:2017 – "Competence, Training, and Conduct Requirements for Regulatory Reviewers"[30] produced by IMDRF. This is IMDRF's Good Regulatory Review Practices (GRRP) document describing criteria "for individuals who perform regulatory reviews of medical devices for marketing authorization," whether those individuals work for governmental regulatory authorities or Conformity Assessment Bodies (CABs)[31] that FDA believes 3P510k ROs and 3PEUA ROs should follow, where applicable, and to the extent such criteria are appropriate and consistent with the FD&C Act and other applicable laws and regulations.

Product Specialist: An individual within a Third Party Review Organization, who meets the criteria of an IMDRF Regulatory Reviewer (defined above), and is qualified to review and evaluate medical devices within specific device type(s), who may also be qualified for a specific technical or clinical specialization (e.g., biocompatibility and sterilization), based on their scientific background and competence. This individual is the primary reviewer responsible for leading the organization's review team on a given 510(k) submission or EUA request. The Product Specialist submits their recommendation and all related documentation to the Final Reviewer.

[30] IMDRF/GRRP WG/N40 Final:2017: "Competence, Training, and Conduct Requirements for Regulatory Reviewers" can be found at http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-competence-conduct-reviewers.pdf

[31] "*Conformity Assessment Body (CAB):* A body other than a Regulatory Authority engaged in determining whether the relevant requirements in technical regulations or standards are fulfilled (GHTF/SG1/N78:2012)", IMDRF/GRRP WG/N40FINAL:2017, section 3.6.

Recognition: The process of accrediting 3P510k Review Organizations under section 523 of the FD&C Act to review premarket notifications submitted under section 510(k) of the FD&C Act of certain eligible devices and make recommendations to FDA regarding the initial classification of such devices under section 513(f)(1) of the FD&C Act.

Rerecognition: The process of renewing the accreditation of 3P510k Review Organizations under section 523 of the FD&C Act. Unless suspended or withdrawn, accreditation is valid for three years.[32]

Recognition Criteria: The applicable FD&C Act requirements, including the qualification requirements set forth in section 523(b)(3) of the FD&C Act; FDA's recommendations described in this guidance document, including those criteria contained in IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews," where appropriate and applicable) and IMDRF GRRP WG N40;[33] and the criteria to accredit or deny accreditation announced in the Federal Register.[34]

Recognition Denial: The process of denying an application for accreditation submitted by a potential 3P510k Review Organization.

Rerecognition Denial: The process of denying an application for reaccreditation submitted by a recognized 3P510k Review Organization.

Recognition Withdrawal: The process of withdrawing or suspending accreditation of a 3P510k Review Organization in accordance with section 523(b)(2) of the FD&C Act.

Safety Signal: A signal that represents a new potentially causal association or a new aspect of a known association between a medical device and an adverse event or set of adverse events.[35]

Submission: As used in this document, "submission" refers to either a 510(k) submission or an EUA request.

Technical Expert: An individual who provides specific knowledge or expertise. This individual may be an employee of a 3P510k Review Organization or 3PEUA Review Organization or may be external as described below in Sections V.B.(2) and V.C.(4) of this guidance, respectively.

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[32] See section 523(b)(2)(D) of the FD&C Act.

[33] IMDRF/GRRP WG/N40 Final:2017: "Competence, Training, and Conduct Requirements for Regulatory Reviewers", previously cited, available at http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-competence-conduct-reviewers.pdf

[34] Medical Devices; Implementation of Third Party Review Under the Food and Drug Administration Modernization Act of 1997; Emergency Processing Request Under OMB Review, 63 FR 28388, May 22, 1998, available at https://www.gpo.gov/fdsys/pkg/FR-1998-05-22/pdf/98-13799.pdf

[35] See Signal Management Program in "Medical Device Safety Action Plan: Protecting Patients, Promoting Public Health," available at https://www.fda.gov/media/112497/download

Third Party 510(k) (3P510k) Review Organization (3P510k RO): An organization recognized by FDA to review 510(k) submissions for certain eligible devices as authorized by section 523 of the FD&C Act.

Third Party EUA (3PEUA) Review Organization (3PEUA RO): An organization under contract with FDA to review EUA requests.

Third Party Review Organization: This phrase refers to either an 3PEUA Review Organization or a 3P510k Review Organization.

V. Third Party Review of 510(k) Submissions and EUA Requests

A. Factors Used in Determining Device Type Eligibility in the 3P510k Review Program

The factors FDA considers in determining device type eligibility for the 3P510k Review Program are as follows:

- The risk of the device type, or subset of such device type.[36] FDA generally classifies medical devices based on risks associated with the device type and whether general controls are sufficient to provide a reasonable assurance of the safety and effectiveness of the device or there is sufficient information to establish special controls to mitigate such risks and provide such assurance. Devices are classified into one of three regulatory classes: class I, class II, or class III.[37] In accordance with the statute, class III devices are not eligible for 3P510k review.[38]
- Whether the device type, or subset of such device type, is intended to be permanently implanted in the human body, to sustain human life, or to support human life. Any 3P510k RO seeking recognition for review of such device types must provide a detailed public health justification explaining why this device type should be eligible for 3P510k review[39] and how this will positively impact public health.
- The extent to which the device type is well understood. For example, devices with novel technological characteristics, including some devices requiring complex special controls initially classified through the De Novo process may be ineligible for 3P510k review.[40]

[36] See section 523(a)(3)(B)(i)(I) of the FD&C Act.
[37] For more information on the classification of medical devices, please visit FDA's website at https://www.fda.gov/about-fda/cdrh-transparency/overview-medical-device-classification-and-reclassification
[38] See section 523(a)(3)(A)(i) of the FD&C Act.
[39] See section 523(a)(3)(B)(i)(II) of the FD&C Act.
[40] See "De Novo Classification Process (Evaluation of Automatic Class III Designation)," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/de-novo-classification-process-evaluation-automatic-class-iii-designation

- The extent to which necessary information to make a well-informed recommendation is available to 3P510k ROs. If information materially relevant to evaluating a device type cannot be shared outside the agency (e.g., it is proprietary), the device type may be ineligible for 3P510k review.
- The extent to which the review of the device type does not require multifaceted, interdisciplinary expertise. The following are examples of scenarios that would likely be ineligible for 3P510k review due to the need for such expertise:

    - The review of some kinds of clinical data or complex non-clinical data (e.g., computational modeling);
    - A need for consultation across different FDA organizational components, or in cross-modality topics (e.g., a multi-reader clinical study);
    - A combination product or device type either of which requires review from another Center in the Agency; and [41]
    - If a device type raises novel cross-labeling considerations, such as the potential for off-label use of drugs (e.g., injector needles or syringes). "Cross-labeled" products usually refer to any drug, device, or biological product packaged separately that, according to its proposed labeling, is for use only with another individually specified drug, device, or biological product where both are required to achieve the intended use, indication, or effect.[42]
    - However, if a device type contains simple clinical data such as sample clinical images or tests using banked specimens, it may be eligible for 3P510k review. Most in vitro diagnostic products are eligible for 3P510k review as they typically rely on simple clinical studies to demonstrate SE, provided that such devices also meet the other factors listed in this section.

- The availability of postmarket data suggesting that the device type is the subject of safety signals. For example, if a device type is the subject of a safety communication, a high-risk recall (Class I)[43], or postmarket data that indicate a safety signal, this device type may be ineligible for 3P510k review.

    For example, duodenoscopes have a safety signal associated with their reprocessing.[44] Because of this safety signal, FDA removed duodenoscopes and accessories from eligibility for the 3P510k Review Program.

FDA will consider each of the above factors in determining device type eligibility for 3P510k review. Furthermore, if a device type is considered eligible for 3P510k review, but a proposed

[41] For more information on combination products, please visit Frequently Asked Questions About Combination Products, available at https://www.fda.gov/combination-products/about-combination-products/frequently-asked-questions-about-combination-products

[42] See the guidance "In Vitro Companion Diagnostic Devices," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/vitro-companion-diagnostic-devices

[43] For more information on classification of recalls, please visit Recalls, Corrections and Removals (Devices), available at https://www.fda.gov/medical-devices/postmarket-requirements-devices/recalls-corrections-and-removals-devices

[44] Information on safety signals associated with duodenoscopes is available at https://www.fda.gov/medical-devices/reprocessing-reusable-medical-devices/infections-associated-reprocessed-duodenoscopes

modification to the device type for a specific submission raises different concerns related to the factors listed above, upon receipt of completed review by a 3P510k RO or through the EI request process outline in Section V.B.(4) of this guidance, FDA may determine that a submission is ineligible for 3P510k review.

If a submitter has previously submitted a 510(k) for a device that resulted in anything other than an SE decision (e.g., withdrew after receiving FDA feedback or was NSE), then that device is not eligible for the 3P510k pathway for that submitter.[45]

The product code classification database[46] and FDA's list of devices eligible for 3P510k review[47] were updated to reflect these eligibility factors to determine 3P510k eligibility for device types. If eligible device types are determined to be ineligible for 3P510k review, or ineligible ones are determined to be eligible for 3P510k review, FDA will change their status in the database and FDA's publicly available list. FDA will periodically review new device types using the factors described above to determine whether they are appropriate for 3P510k review, and update the database and list accordingly.

B. Review of 510(k) Submissions or EUA Requests by Third Party Review Organizations

FDA believes that Third Party Review Organizations should conduct FDA-equivalent reviews of appropriate devices. Third Party Review Organizations are responsible for reviewing and analyzing scientific and technical data in a submission to make a recommendation to FDA regarding the device. Third Party Review Organizations should conduct their review of submissions in the manner described in the sections below and in accordance with their own quality control practices. Figure 3 identifies the key steps in a 3P510k RO's review of a 510(k) submission,[48] while Figure 4 identifies the key steps in a 3PEUA RO's review of an EUA request.

[45] See section 523(a)(3)(B)(iii) of the FD&C Act.
[46] The product code classification database is available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm
[47] A current list of eligible devices for 3P510k review is available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfThirdParty/current.cfm
[48] Figure 3 uses IEC/IEC 19510: Information technology – Object Management Group Business Process Model and Notation (2013).

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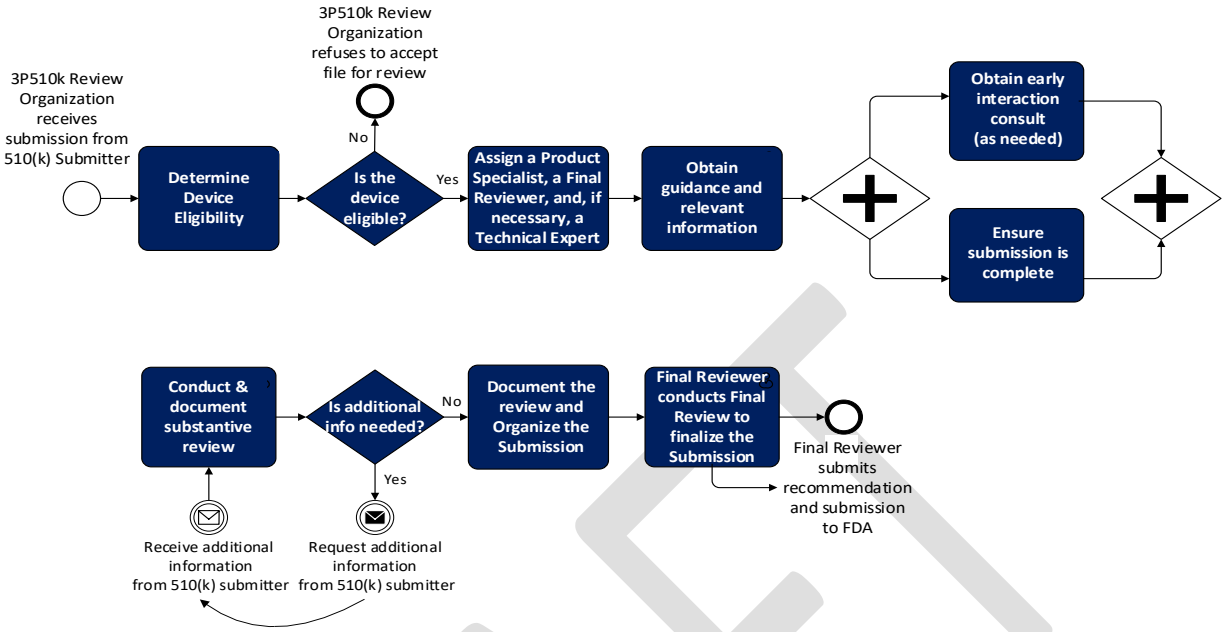

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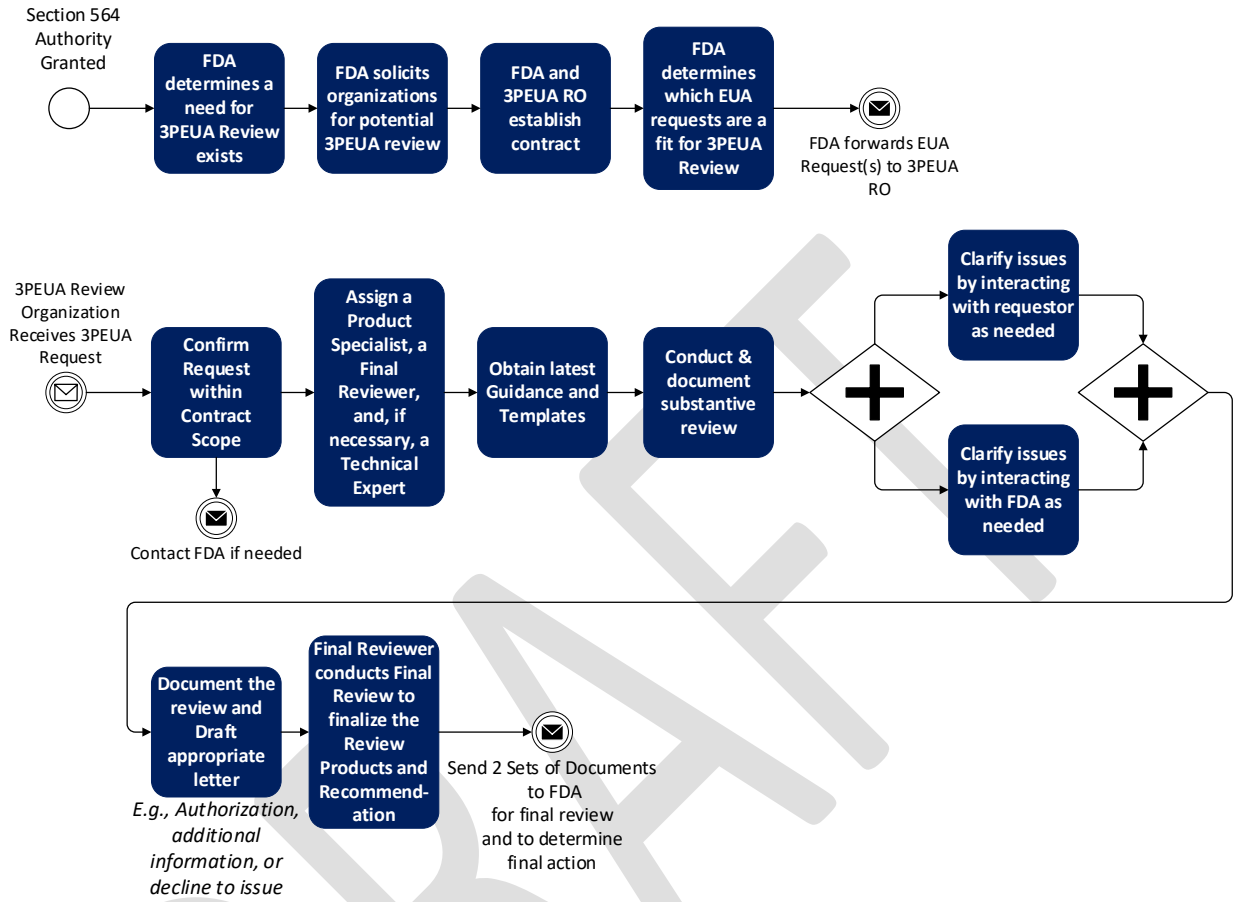
Figure 4: Steps in Establishing and Conducting EUA Review by a 3PEUA Review Organization



(1) Determine device eligibility

Before reviewing a 510(k) submission, a 3P510k RO should determine whether they have the expertise to review the device type and whether that device type is eligible for 3P510k review based on review of the product code classification database[49] or the FDA Third Party Review public website.[50] If the 3P510k RO lacks the expertise or the device is not eligible for 3P510k review, the 3P510k RO should not accept the 510(k) submission for review from the 510(k) Submitter. If the 3P510k RO determines the device is ineligible for 3P510k review after they have already accepted the 510(k) submission, the 3P510k RO should immediately inform the 510(k) Submitter and discontinue the review.

[49] The product code classification database is available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm

[50] The list of eligible devices for third party review under the 3P510k Review Program is available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfThirdParty/current.cfm

3P510k ROs should establish policies designed to identify, prevent, and ensure reporting to FDA instances of forum shopping by 510(k) Submitters. 510(k) Submitters who consult with more than one 3P510k RO in order to find a review organization that is most likely to recommend clearance of a 510(k) submission undermine the independence and integrity of the 3P510k Review Program. 3P510k ROs should take steps to ensure that the submitters of the 510(k)s they are reviewing have not previously presented the submission to another RO and have not modified their device description or intended use to be reviewed by a different review office in FDA.

If the 3P510k RO submits a 510(k) submission to FDA for an ineligible device, or a device the 3P510k RO is not recognized to review (see Section V.D.(1) of this guidance), FDA will place the submission on hold and notify the 3P510k RO of FDA's eligibility assessment. Unless the 3P510k RO intends to address the eligibility concerns, they should promptly consult with the 510(k) Submitter and, if the 510(k) Submitter concurs, promptly send a 510(k) withdrawal request to FDA. If the 3P510k RO does not address eligibility concerns or withdraw the submission within 180 days, FDA will delete the file. A 510(k) Submitter cannot submit a 510(k) for the same device directly to FDA or to another 3P510k RO until the file is withdrawn voluntarily by the 3P510k RO or deleted automatically by FDA after 180 days. If a 3P510k RO has questions about the eligibility status of a device, they should contact the 3P510k mailbox at 3P510K@fda.hhs.gov to seek clarification.

A 3PEUA RO should likewise review an EUA request to ensure that it is appropriate for 3PEUA review regardless of whether the EUA request is sent from FDA or directly from the EUA Submitter. This includes assessing whether the device is within the purview of the organization's contract with FDA (e.g., confirming the device type and intended use). If the EUA request is not appropriate for third party review, the 3PEUA RO should inform FDA.[51] If the EUA request is for an in vitro diagnostic product that was sent by the EUA Submitter directly to the 3PEUA RO, the 3PEUA RO should inform FDA and the EUA Submitter's designated correspondent. A 3PEUA RO may communicate with FDA to confirm its assessment before informing the EUA Submitter.

(2) Assign a Product Specialist(s), Final Reviewer, and Technical Expert(s) to conduct the substantive review of a submission

Third Party Review Organization personnel should have appropriate education, training, skills, technical knowledge, qualifications, and experience to perform submission reviews for the device type(s) their organization is recognized and/or contracted to review. For additional discussion on FDA's recommendations regarding qualifications of personnel, see Section V.C.(2) of this guidance.

Each submission should be assigned to a Product Specialist with appropriate expertise for the type of device under review. The Product Specialist may add qualified Technical Experts to the review team to ensure sufficient competency in the review, if necessary. The Product Specialist

[51] FDA will provide a designated email address when issuing the final guidance.

should document the competencies of, and the rationale for, choosing to use any Technical Experts. Particular attention should be given to the expertise and impartiality of any external Technical Experts. For more information on using external Technical Experts, please see Section V.C.(3) of this guidance.

Third Party Review Organizations should also identify at least one Final Reviewer within its organization who is independent from prior review of the submission and is responsible for providing a final supervisory assessment of the Product Specialist's work before it is submitted to FDA. This individual should have sufficient authority and competence to independently assess the quality and acceptability of the Product Specialist's review of the submission.

(3) Obtain relevant FDA guidance(s) and information

Third Party Review Organizations should review and be familiar with publicly available information relevant to their review. For example:

- Third Party Review Organizations should review FDA's guidance database to obtain any relevant final guidance documents[52] when conducting their reviews, including device-specific and horizontal guidances (e.g., biocompatibility, software, sterility).
    - 3P510k ROs should be aware of any special controls, which are regulatory requirements for certain class II devices, that apply to that device type under review. For information on whether a device type has applicable special controls, 3P510k ROs should review the regulation associated with the device's proposed classification under Title 21 of the Code of Federal Regulations (CFR),[53] which will identify the mandatory special controls for a particular device type.
    - For 3PEUA ROs conducting reviews specific to an applicable EUA declaration, FDA's Emergency Preparedness and Response website[54] may provide additional information (e.g., EUA templates to assist EUA Submitters in preparing their requests).
- 3P510k ROs should review FDA's postmarket databases, including recalls, market withdrawals, and safety reports;[55] Medical Device Reports;[56] and MedSun Reports[57] for the predicate device and/or the device type to identify any issues with clinical use of similar devices that should be considered and addressed in the review of the subject device. If potential safety signals are identified by a 3P510k RO, they should contact FDA for information on current review practice (see Section V.B.(4) of this guidance).

[52] The guidance database search engine allows users to search the inventory of guidances available by title, words, or origin and is available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents

[53] The Code of Federal Regulations Title 21 database is available at https://www.ecfr.gov/cgi-bin/ECFR?page=browse

[54] Available at https://www.fda.gov/emergency-preparedness-and-response

[55] The recalls database allows users to search for recalls and correction or removal actions initiated by a firm prior to recall classification and is available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfRES/res.cfm

[56] The MAUDE database allows users to search for Medical Device Reports and is available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfMAUDE/TextSearch.cfm

[57] The MedSun database allows users to search for adverse event reports from the Medical Product Safety Network and is available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/Medsun/searchReportText.cfm

- 3P510k ROs should review publicly available premarket review information in FDA's 510(k) database for information about the legally marketed device ("predicate") to which a Submitter is comparing its device, or other similar devices,[58] including Indications for Use Statements, 510(k) Summaries,[59, 60] Decision Summaries, if available, and FDA decision letters. In some instances, a device's product code can also be used to identify a generic category of a device and assist with the identification of similar devices. Product codes can be found in FDA's product code database.[61]

- If a submitter wishes to utilize standards, the Third Party Review Organization should review FDA's guidance document entitled "Appropriate Use of Voluntary Consensus Standards in Premarket Submissions for Medical Devices."

Third Party Review Organizations should request that submitters fully inform them of any prior communications with FDA about a device under review, including but not limited to FDA feedback obtained through the Q-Submission program, Pre-EUAs, unsuccessful marketing applications, and other interactions. If applicable, 3P510k ROs should be familiar with the FDA Q-Submission Program, including the Pre-Submission process, through the guidance document entitled, "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program."[62] A 3P510k RO should request an authorization letter from the 510(k) Submitter granting FDA permission to share information about or from previous submissions with the 3P510k RO (e.g., Q-Submissions and 510(k)s) related to the device (see Section V.B.(9) of this guidance). If applicable, the Third Party Review Organization should coordinate with the submitter to obtain and review prior submission content for the device, any written feedback or meeting minutes resulting from prior interactions, and any additional data, studies and/or study protocols submitted in response to previous submissions prior to the current submission to FDA.

FDA will review only one submission for a device at a time. Therefore, 3P510k ROs should confirm that 510(k) Submitters submit only one submission for a specific device at a time. If a 3PEUA RO receives an EUA request directly from a submitter, they should similarly check with FDA, through the 3PEUA mailbox that will be included in the final guidance, to ensure that a submission for the same device was not also submitted directly to FDA.

(4) Early Interaction with FDA

[58] The 510(k) database search engine allows users to search all previously cleared 510(k) submissions by 510(k) number, applicant name, device name, product code, etc., and is available on FDA's website at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm

[59] See 21 CFR 807.92.

[60] See also the guidance "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]."

[61] The product code database is available on FDA's website at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/classification.cfm

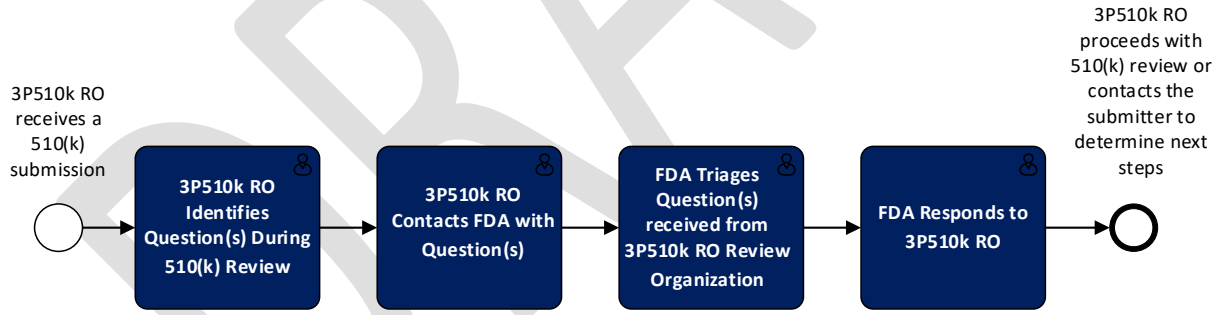
[62] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program

Third Party Review Organizations should interact, as needed, with appropriate FDA staff prior to and during the review of submissions. For 3P510k review, EIs – those between the 3P510k RO and FDA prior to the substantive review – can be an important part of the 510(k) review process (for potential topics, refer to Section V.B.(4) of this guidance). These interactions help ensure timely and consistent 510(k) reviews by assisting in device eligibility determinations and identifying relevant issues and contemporary review criteria.

In their initial recognition applications, 3P510k ROs commit to EIs with FDA before reviewing a device type they have not previously reviewed (see Section V.D.(1) of this guidance). This interaction ensures that the 3P510k RO has the latest FDA thinking on relevant guidance, standards, and other considerations for that device type. FDA encourages EIs for all 3P510k submissions, particularly for the first review of any device type by an individual Product Specialist and for any subset of device type (i.e., device type by product code) they have not recently reviewed. Generally, FDA considers a recent review to be within the last six months.

Procedures on how to obtain EI are available on FDA's "510(k) Third Party Review Program" website. The 3P510k Program Review Team intends to respond to 3P510k RO requests within 2 business days of receipt of an EI request. The 3P510k Program Review Team intends to triage the EI request before sending to the appropriate review division. If that deadline cannot be met, FDA intends to work with the 3P510k RO to establish a reasonable timeline for a response. Each review division within FDA that receives an EI intends to respond within 7 calendar days.

Figure 5. 3P510k RO's Steps to Interacting Early with the FDA



To enable FDA to provide timely feedback to 3P510k ROs through this process, the EI should be succinct and focused on one or two key questions if possible. Focused key questions include asking FDA to clarify a particular issue for the 3P510k RO, such as whether the software in a device should be evaluated as a low risk or a high risk, or whether the product code in the submission (include the device description) is correct or if FDA would expect the device to be regulated under a different product code. The EI may ask whether FDA recommends additional testing for a device beyond what is reflected in the 510(k) summary of the predicate device. Please note that an EI should also include the 3P510k RO's proposed resolution of the issue. If an EI is overly broad or too detailed, FDA may be unable to provide feedback but will try to work with the 3P510k RO to focus on the key issue in the organization's review.

FDA recommends EIs if there are questions about whether the submission is for a known device type with novel technology (e.g., addition of artificial intelligence/machine learning (AI/ML)) or whether the submission is appropriate for 3P510k review (e.g., possible data integrity issues).

For 3PEUA questions, rather than resorting to the EI process, 3PEUA ROs should check in regularly with FDA to remain up to date on any emerging understanding, templates, or expectations relevant to EUA review.

(5) Ensure a submission is administratively complete

To ensure that a submission is administratively complete, 3P510k ROs should conduct a review of the 510(k) submission based on 510(k) regulations from 21 CFR Subpart E to assess whether the 510(k) submission includes all the information necessary to conduct a substantive review and to reach a recommendation (i.e., SE or NSE) to submit to FDA.

The 510(k) submitter should utilize the electronic Submission Template and Resource (eSTAR) to facilitate the preparation of 510(k) submissions to make sure a submission is administratively complete. For more information on eSTAR, please see Section V.B.(9) of this guidance and the "Electronic Submission Template for Medical Device 510(k) Submissions" guidance.[63]

3PEUA ROs should likewise ensure that an EUA request has enough information to enable review before conducting a substantive review. The exact type and amount of data needed to support an EUA may vary depending on the nature of the declared emergency or threat of emergency and the nature of the candidate product.[64] FDA anticipates that expectations of requests will be detailed at the time a contract is awarded for 3PEUA review as well as where or with whom to check for updates to that information. If the correspondent is not the manufacturer, but is acting on behalf of the manufacturer, the submission should include authorization for the correspondent to act on behalf of the manufacturer. This does not change who FDA considers to be the EUA Submitter. If FDA has posted on its website specific information recommended for the device type being reviewed (e.g., FDA posted a template for EUA requests for SARS-CoV-2 antigen tests), it may be a helpful reference for this assessment.

Third Party Review Organizations should not act as a consultant for the submitter. It is the responsibility of the submitter to be familiar with the content and format requirements of a 510(k) submission or EUA request prior to submitting to FDA or a Third Party Review Organization. If a submitter is not familiar with the 510(k) regulatory pathway, 3P510k ROs should direct them to resources such as FDA's guidance documents entitled, "The 510(k)

[63] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/electronic-submission-template-medical-device-510k-submissions. As of October 1, 2023, 510(k) submissions are required to be submitted electronically using eSTAR unless meeting a criteria for waiver or exemption.

[64] See "Emergency Use Authorization of Medical Products and Related Authorities," available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities

Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]," "The Abbreviated 510(k) Program," and "The Special 510(k) Program." If an EUA Submitter is not familiar with the process for obtaining authorization for emergency use of a device, the 3PEUA RO should direct them to resources such as FDA's guidance document entitled, "Emergency Use Authorization of Medical Products and Related Authorities" or FDA's Emergency Use Authorization website. Third Party Review Organizations might also direct submitters to the Division of Industry and Consumer Education in the Office of Communication and Education.

If the Third Party Review Organization determines that a submission is administratively complete, the organization should begin its substantive review of the submission. If the Third Party Review Organization identifies any deficiencies in the submission, they should contact the submitter to request the missing information.

(6) Conduct the substantive review of a submission

Substantive review will be different for 510(k) submissions and EUA requests.

Substantive review for 510(k)s focuses on the evaluation of SE as defined in section 513(i) of the FD&C Act. 21 CFR 807.100(b) sets forth the criteria that FDA uses to determine whether a device is substantially equivalent to a legally marketed device. For information on making an SE determination under the 510(k) program, please see FDA's guidance document entitled "The 510(k) Program: Evaluating Substantial Equivalence in Premarket Notifications [510(k)]." For information on Abbreviated and Special 510(k)s, see FDA's guidance documents entitled "The Abbreviated 510(k) Program" and "The Special 510(k) Program."

Review of an EUA request assesses the potential effectiveness of a possible EUA product on a case-by-case basis using a benefit-risk analysis. If, based on the totality of the scientific evidence available, it is reasonable to believe that the product may be effective for the specified use, FDA may authorize its emergency use, provided that other statutory criteria for issuing an EUA also are met. To enable FDA to reach a determination on whether to issue an EUA, the reviewer needs to document their assessment with particular attention to sections 564(c)(2)(A) and 564(c)(2)(B) of the FD&C Act. The 3PEUA RO review and recommendation should include

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[65] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k

[66] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/abbreviated-510k-program

[67] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/special-510k-program

[68] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities

[69] See FDA's Emergency Use Authorization website at https://www.fda.gov/emergency-preparedness-and-response/mcm-legal-regulatory-and-policy-framework/emergency-use-authorization

[70] The contact information for the Division of Industry and Consumer Education is available at https://www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/contact-us-division-industry-and-consumer-education-dice

[71] See the guidance "Emergency Use Authorization of Medical Products and Related Authorities."

those materials appropriate to the conditions of authorization discussed in Appendix A of the "Emergency Use Authorization of Medical Products and Related Authorities" guidance.[72] The review and recommendation should also include a proposed indication for use. For example, an in vitro diagnostic product indication would typically include the sample type, the disease or condition being tested, when the test should be administered (e.g., within N days of symptoms or to anyone suspected of exposure), and by whom it can be used (e.g., a laboratory that meets the requirements to perform high or moderate complexity tests). FDA makes its own determinations – and does not intend to seek recommendations from 3PEUA ROs – regarding whether other criteria for issuance are satisfied, including whether the agent that is the subject of the EUA declaration can cause a serious or life-threatening disease or condition under section 564(c)(1) of the FD&C Act and whether there is an adequate, approved, and available alternative to the product under section 564(c)(3) of the FD&C Act.

The Final Reviewer is responsible for providing a final supervisory assessment of the Product Specialist's work before it is submitted to FDA. This individual should have sufficient authority and competence to independently assess the quality and acceptability of the Product Specialist's review of the 510(k) submission.

If Third Party Review Organizations identify any deficiencies during their substantive review, they should contact the submitter with a request that the deficiencies be addressed. Section V.B.(7) below provides further instruction on how to identify deficiencies in a submission. When the substantive review is complete, the Product Specialist(s), Technical Expert(s), if applicable, and Final Reviewer should reach an agreement on a final recommendation (e.g., SE or NSE to a predicate device for a 510(k) or authorization for an EUA[73]) before submitting the recommendation to FDA.

(7) Identify deficiencies in a submission

If a Third Party Review Organization identifies any deficiencies during their review, it should contact the submitter. Third Party Review Organizations may use any form of communication (e.g., telephone, email, or letter) to resolve the matter provided confidentiality is maintained and the interaction is documented. Third Party Review Organizations should, however, avoid the exchange of substantive data and information solely over the telephone to avoid errors that may arise in the absence of a written request and response.

As part of providing an FDA-equivalent review, when requesting additional information from a 510(k) Submitter, 3P510k ROs should structure their additional information requests as described in FDA's guidance document entitled "Developing and Responding to Deficiencies in Accordance with Least Burdensome Provisions."[74] This guidance document has examples of

[72] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/emergency-use-authorization-medical-products-and-related-authorities#appA

[73] See sections 564(e)(1) or 564(e)(2) of the FD&C Act.

[74] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/developing-and-responding-deficiencies-accordance-least-burdensome-provisions

well-constructed deficiencies and responses to FDA's requests. Note that while the guidance cited does not apply to EUAs, it is important that 3PEUA ROs also request additional information in a clear and structured format.

Third Party Review Organizations should document the deficiencies, the submitter's response to the deficiencies, and the discussion on the adequacy of the response in the Third Party Review Organization's review memorandum sent to FDA. With the review memorandum, a copy of all written communications related to resolving the deficiencies between the submitter and the Third Party Review Organization (e.g., email, letters, summary of teleconferences) should also be provided to the FDA. If the submitter made any modifications to the submission in response to a deficiency (e.g., revised 510(k) summary), the Third Party Review Organization should document this modification. Further, the Third Party Review Organization should request that the submitter provide the latest version of the submission prior to the Third Party Review Organization submitting to FDA. For example, if the Product Specialist requested an updated device description, the latest version should be included when the Third Party Review Organization sends the submission to FDA. However, the original device description text and the deficiency requesting an updated device description should be provided with the review memo. This will help ensure that FDA has the correct version of the submission on record. Proper documentation can also help address any appearance of the Third Party Review Organization having the role of a consultant.

(8) Document a review

Once a Third Party Review Organization has made a final recommendation, they should prepare their review documentation specifying the reasoning and steps that led to their final recommendation. 21 CFR 10.70 ("Documentation of significant decisions in administrative file") provides a framework that should be utilized by Third Party Review Organizations. The content of the review documentation will vary based on the type of submission and device. Recommended review memorandum examples for documentation purposes are available on the FDA Third Party public website.[75] The review memo should provide a clear narrative of: (1) how the device works; (2) for a 510(k), what information the submitter provided to demonstrate the device is SE to a legally marketed device, or, for an EUA request, based on the totality of the scientific evidence available, what information the submitter provided to demonstrate it is reasonable to believe that the product may be effective for the specified use; and (3) how the Third Party Review Organization evaluated that information.

If standards are referenced in a submission, FDA recommends Third Party Review Organizations discuss in their review memorandum how they were utilized in the submission. Submitters and Third Party Review Organizations should consult the FDA guidance entitled, "Appropriate Use

[75] See FDA's third party website: https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/510k-third-party-review-program

of Voluntary Consensus Standards in Premarket Submissions for Medical Devices"[76] for use of FDA-recognized consensus standards and use of other standards.

In addition to noting whether or not the necessary information required in a submission was included,[77] the review memorandum should also convey how a Third Party Review Organization made their recommendation regarding the device. A thorough and substantive review memorandum should discuss the adequacy of each section of the submission. In general, FDA believes it will not be sufficient to state that a section of the submission or a response to a deficiency was adequate without providing an explanation of how the Third Party Review Organization came to that determination.

To facilitate FDA's review process, Third Party Review Organizations should reference sections and page numbers of the submission in their review memorandum where possible. Third Party Review Organizations should also clearly document in the review memorandum any deficiencies, the response to the deficiencies, and the Third Party Review Organization's review of the response as indicated in Section V.B.(7) of this guidance.

The review memorandum is the only means by which FDA can understand how and why a Third Party Review Organization recommended a device to be SE (or NSE) to the predicate device or receive an EUA. It is anticipated that thorough and clear documentation will reduce the need for FDA to re-review the submission itself and increase the efficiency of FDA's final review.[78]

(9) Organize and submit a submission including associated Third Party Review Organization review documentation

Upon completing the review of a submission, the Third Party Review Organization should submit the following to FDA:

- The submission generated by the submitter, and
- The review documentation generated by the Third Party Review Organization.

Submissions will need to follow the appropriate submission process.[79]

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[76] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices

[77] See 21 CFR 807 Subpart E.

[78] Through the MDUFA IV Commitment Letter, FDA commits to improving the Third Party Review Program with a goal of eliminating routine re-review by FDA of third party reviews: See 163 CONG. REC. S4729-S4736 (daily ed. August 2, 2017) (Food and Drug Administration User Fee Reauthorization), also available at https://www.fda.gov/media/102699/download. Through the MDUFA V Commitment Letter, FDA commits to the continued improvement of the Third Party Review Program with a goal of eliminating routine re-review by FDA of third party reviews: See 168 CONG. REC. S5195-S5200 (daily ed. September 28, 2022) (Food and Drug Administration User Fee Reauthorization), also available at https://www.fda.gov/media/158308/download. See also "Eliminating Routine FDA Re-Review of Third Party 510(k) Reviews," available at https://www.fda.gov/media/116168/download

[79] For 510(k)s see FDA's website on the 510(k) submission process, available at https://www.fda.gov/medical-devices/premarket-notification-510k/510k-submission-process

The 510(k) Submitter's document and the 3P510k RO's documents must be in electronic format per section 745A(b)(2) of the FD&C Act unless it meets the criteria for exemptions and waivers.[80] The electronic submission template, eSTAR, is the only currently available electronic submission template to facilitate the preparation of 510(k) electronic submissions. The 510(k) Submitter should take care to submit the latest version of the 510(k) submission to the 3P510k RO. This version should include any documents that have been updated in response to deficiencies from the 3P510k RO. The 3P510k RO will submit all documents to FDA via the directions outlined on the CDRH Portal.[81]

For 3PEUA submissions, unless otherwise requested by FDA, the 3PEUA RO should submit files to the CDRH Portal or CDRH's Document Control Center.[82] In the event that the EUA Submitter has amended their original submission during the 3PEUA review, or the submission was sent directly to the 3PEUA RO, the 3PEUA RO should submit two separate sets of files, one set for the updated EUA request and one for the 3PEUA RO's review of the EUA request. In the case where the original EUA request was sent to FDA and it does not need amending, the 3PEUA Final Reviewer need only submit their review files. Please refer to FDA's guidance entitled "eCopy Program for Medical Device Submissions"[83] for more information on how to submit through the eCopy program.

To facilitate FDA's review, we recommend that a Third Party Review Organization's documentation include the following:

For both 3P510k ROs and 3PEUA ROs:

- A cover letter signed by the Final Reviewer that clearly identifies:
  - The purpose of the submission, e.g., a new 3P510k review and submission, a new 3PEUA review and submission, a Third Party Review Organization's review to an existing 510(k) or EUA submission number provided by FDA–in this case clearly indicate the 510(k) or EUA submission number;
  - The name and address of the Third Party Review Organization and the contact person;
  - The name, email, and telephone number of the Final Reviewer;
  - The name and address of the submitter;

[80] As noted in the guidance "Electronic Submission Template for Medical Device 510(k) Submissions," all 510(k) submissions including original submissions for Traditional, Special, and Abbreviated 510(k)s, and subsequent Supplements and Amendments and any other subsequent submissions to an original submission, unless exempted in Section VI.A Waivers and Exemptions From Electronic Submission Requirements of the guidance, are required to be submitted as electronic submissions.

[81] The CDRH Portal is available at https://www.fda.gov/medical-devices/industry-medical-devices/send-and-track-medical-device-premarket-submissions-online-cdrh-portal

[82] CDRH's Document Control Center is available at https://www.fda.gov/medical-devices/how-study-and-market-your-device/ecopy-program-medical-device-submissions

[83] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/ecopy-program-medical-device-submissions

  - The name of the device (trade name, common or usual name, FDA classification regulation name, classification regulation number, and product code, as applicable);
  - The Third Party Review Organization's recommendation (SE or NSE, authorization) with respect to the device; and
  - For submissions sent directly to Third Party Review Organizations by submitters, the date when the submission was judged administratively complete and ready for substantive review.
- A signed certification that the reported information accurately reflects the data reviewed and that no material fact has been omitted. This certification should also state that the Third Party Review Organization continues to meet personnel qualifications and prevention of conflicts of interest criteria reviewed by FDA; that the Third Party Review Organization's review is based on the submission that is being submitted with the review; and that the Third Party Review Organization understands that the submission of false information to the government is prohibited by 18 U.S.C. 1001 and 21 U.S.C. 331(q).
- The submitter's complete submission. The submission should be prepared by the submitter, not the Third Party Review Organization. This information should be separate from the Third Party Review Organization's documentation and should be the latest version (see Section V.B.(7) of this guidance for more information). Proper documentation can help address any appearance of the Third Party Review Organization having the role of a consultant.
  - For 510k submissions: The submission should conform to FDA's requirements for content and format as provided in 21 CFR part 807 subpart E and utilize eSTAR.
- A review memorandum including complete documentation of the Third Party Review Organization's review of the submission as described in Sections V.B.(7) and V.B.(8) of this guidance, signed by all personnel who conducted the review (generally the Product Specialist(s), Technical Expert(s), when applicable, and Final Reviewer), with a decision recommendation.

For 3P510k ROs:

- A review of the 510(k) submission contents that show the submission was administratively complete and includes all of the information necessary for the 3P510k RO to conduct a substantive review on FDA's behalf. A summary of any EI consults that occurred prior to the 510(k) submission to FDA with FDA staff, if appropriate (see Section V.B.(4) of this guidance).

For 3PEUA ROs:

- A review of the EUA request contents to show that the EUA request includes all of the information necessary for the 3PEUA RO to conduct a substantive review on FDA's behalf. If a template exists for the device type, it may be a helpful reference for this assessment.

For submissions submitted directly to Third Party Review Organizations:

- For 510(k)s : A letter signed by the 510(k) Submitter authorizing the 3P510k RO to submit the 510(k) to FDA on their behalf and authorizing the 3P510k RO to discuss the

contents of the 510(k) with FDA on their behalf. This letter should also authorize FDA to discuss other, related submission(s) from the same 510(k) Submitter with the 3P510k RO and should include a list of those submission numbers.

FDA will begin its review of the Third Party Review Organization's recommendation only after we receive all documentation we believe is needed to conduct its review.

(10) Submit additional information upon FDA's request

After a Third Party Review Organization has submitted their recommendation to FDA, including the associated Third Party Review Organization review documentation, FDA will begin to review the Third Party Review Organization review documentation, and if necessary, the submission. If FDA determines that additional information is needed to make a final decision (i.e., an SE determination or authorization), we will contact the Third Party Review Organization either by telephone or email.[84] Such requests will describe FDA's concerns with a submission, and identify the information needed to address those concerns.

If FDA places a submission "on hold" (i.e., officially suspends review of the submission pending FDA's receipt of additional information), we will send an email informing the Third Party Review Organization of the "on hold" status and request additional information. For more information on a request for additional information for a 510(k) submission, please see FDA's guidance entitled "FDA and Industry Actions on Premarket Notification (510(k)) Submissions: Effect on FDA Review Clock and Goals."[85]

Upon receiving a request from FDA for additional information, the Third Party Review Organization should:

- Promptly inform the submitter of FDA's request for additional information relating to the submission and request that the submitter provide responses to the Third Party Review Organization in writing. The Third Party Review Organization should be involved in any discussions with FDA regarding the request for additional information, such as if the submitter seeks clarification from FDA or a 510(k) Submitter requests a Submission Issue Meeting[86] with FDA;
- Thoroughly review any additional information provided by the submitter to ensure that it adequately responds to FDA's concerns;
- Document their review of the response to the deficiency by providing a clear and thorough assessment of whether and how the response adequately addresses FDA's deficiency – this should include updating the review documentation accordingly;

[84] Through the MDUFA V Commitment Letter, FDA will continue to support the Third Party Review program, with the objective of eliminating routine re-review by FDA of Third Party reviews: See 168 CONG. REC. S5195-S5200 (daily ed. September 28, 2022) (Food and Drug Administration User Fee Reauthorization), also available at https://www.fda.gov/media/158308/download

[85] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/fda-and-industry-actions-premarket-notification-510k-submissions-effect-fda-review-clock-and-goals

[86] See the guidance "Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program."

- Prepare a cover letter referencing the submission number previously assigned by FDA (i.e., 510(k) number or EUA number) and identifying the purpose of the new submission (i.e., response to deficiencies); and

- For 510(k)s, send an updated eSTAR via the CDRH Portal, and for EUAs, send any update to the CDRH Portal, the CDRH's Document Control Center or as otherwise indicated by FDA.

The Third Party Review Organization should provide to FDA the two separate sets of documents[87] (the new submission document(s) generated by the submitter and the document generated by the Third Party Review Organization). Each set of documents should be clearly marked as belonging to the Third Party Review Organization or the submitter as appropriate. For information on formatting requirements, see Section V.B.(9) of this guidance.

FDA will resume its review after we receive the submitter's response to the additional information request, documentation of the Third Party Review Organization's review, and the Third Party Review Organization's determination of the adequacy of the response to additional information requests.

(11) Submission dispute resolution

Disputes may often be the result of misunderstanding or miscommunication, and FDA encourages Third Party Review Organizations to seek clarification, as needed, from FDA or the submitter during a review. In some cases, the misunderstanding may result from FDA making a determination based in part on information that is available to FDA but is not available to the Third Party Review Organization (e.g., other premarket submissions from the submitter). If the submitter disagrees with an FDA decision or action, the Third Party Review Organization should maintain impartiality and exercise care to avoid the appearance of conflict of interest that may result from acting or appearing to act as an advocate on the submitter's behalf.

For 510(k) submissions, FDA has developed guidance documents that provide an overview of the appeals processes available for medical devices, see "Center for Devices and Radiological Health Appeals Processes"[88] and "Center for Devices and Radiological Health Appeals Processes: Questions and Answers About 517A."[89] The processes for reviewing and reconsidering FDA decisions or actions on other 510(k) submissions are also available for 3P510k submissions when a dispute between FDA and a 510(k) Submitter arises.

If a 510(k) Submitter would like to issue a complaint against a 3P510k RO, communication should be sent to 3P510K@fda.hhs.gov.

[87] See the guidance "eCopy Program for Medical Device Submissions."
[88] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/center-devices-and-radiological-health-cdrh-appeals-processes
[89] Available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents/center-devices-and-radiological-health-cdrh-appeals-processes-questions-and-answers-about-517a

C. FDA Expectations of Third Party Review Organizations and for Recognition and Rerecognition of 3P510k Review Organizations

FDA considers criteria when deciding to recognize 3P510k ROs to conduct premarket reviews of eligible 510(k)s.

In accordance with section 523(b)(3) of the FD&C Act, a 3P510k RO shall, at a minimum, meet the following qualification requirements. Such person:

- May not be an employee of the Federal Government;
- Shall be an independent organization, which is not owned or controlled by a manufacturer, supplier, or vendor of devices, and which has no organizational, material, or financial affiliation with such a manufacturer, supplier, or vendor;
- Shall be a legally constituted entity permitted to conduct the activities for which it seeks recognition;
- Shall not engage in the design, manufacture, promotion, or sale of devices;
- The operations of such person shall be in accordance with generally accepted professional and ethical business practices; and
- Shall agree, at a minimum, to include in its request for accreditation a commitment to, at the time of accreditation, and at any time it is performing any review pursuant to section 523:
    - Certify that reported information accurately reflects data reviewed;
    - Limit work to that for which competence and capacity are available;
    - Treat information received, records, reports, and recommendations as proprietary information;
    - Promptly respond and attempt to resolve complaints regarding its activities for which it is recognized; and
    - Protect against the use, in carrying out the review of a 510(k) submission and initial classification of a device, of any officer or employee of the person who has a financial conflict of interest regarding the device, and annually make available to the public disclosures of the extent to which the 3P510k RO, and the officers and employees of the 3P510k RO, have maintained compliance with requirements relating to financial conflicts of interest.

Congress directed FDA to issue guidance on consultations with third party reviewers of EUAs under section 565(i) of the FD&C Act, "including considerations concerning conflicts of interest."[90] Consistent with this directive and existing policy with respect to 3PEUA review of medical devices, including in vitro diagnostic products, FDA will take into consideration the potential for financial conflicts of interest regarding the device.

In addition to these minimum requirements set forth in section 523(b)(3) of the FD&C Act, a Third Party Review Organization should also consider any additional qualifications applicable to

[90] See section 2502(b) of the FY 2023 Omnibus.

its type of review that are announced in the Federal Register. For 3P510k ROs, these qualifications include establishing policies designed to identify, prevent, and ensure reporting to FDA of instances where 510(k) Submitters submit substantially the same submission to multiple 3P510k ROs in order to find the one most likely to recommend a SE determination of the 510(k) submission. Such forum shopping would undermine the independence and integrity of the 3P510k Review Program.[91]

(1) Operational considerations

All submissions and communications with FDA and all documentation pertaining to the review of a 510(k) or EUA submission submitted to FDA should be in English.

(2) Management of impartiality

FDA expects Third Party Review Organizations to be impartial and free from any commercial, financial, and other pressures that might present a conflict of interest or an appearance of a conflict of interest. Therefore, FDA will consider whether the potential Third Party Review Organization has established, documented, and executed policies and procedures to prevent any individual or organizational conflict of interest or the appearance of a conflict of interest, including conflicts of interests pertaining to their external Technical Experts. Policies and procedures intended to address this issue should be consistent with IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews[92] and IMDRF GRRP WG/N40 FINAL:2017 – "Competence, Training, and Conduct Requirements for Regulatory Reviewers."[93] For more information on IMDRF GRRP and MDSAP, see Section V.F of this guidance below.

FDA recommends that Third Party Review Organizations also address the following to prevent a potential conflict of interest:

- Third Party Review Organizations should not participate in the preparation of submissions. For more information, see Section V.B.(5) of the guidance.
- Third Party Review Organizations should not task an individual, whether employee or contractor, with reviewing a submission, if that individual was employed within the last twelve months by that submitter or by a firm who helped prepare that submission.

[91] As noted in Medical Devices; Implementation of Third Party Review Under the Food and Drug Administration Modernization Act of 1997; Emergency Processing Request Under OMB Review, 63 FR 28390, May 22, 1998, available at https://www.gpo.gov/fdsys/pkg/FR-1998-05-22/pdf/98-13799.pdf

[92] IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews" can be found at https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-200318-rrar-cab-cmdrr-n59.pdf

[93] IMDRF GRRP WG/N40 Final:2017: "Competence, Training, and Conduct Requirements for Regulatory Reviewers" can be found at http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-competence-conduct-reviewers.pdf

Personnel should not review a medical device that they developed, helped develop, or prepared for submission.

- Third Party Review Organizations should not promise or advertise any guarantees for FDA clearance or authorization.

Information on the conflict of interest standards FDA applies to its own review personnel is included in the document entitled "Standards of Ethical Conduct for Employees of the Executive Branch."[94] Third Party Review Organizations are encouraged to refer to these standards in safeguarding their operations against conflicts of interest.

The conflict of interest policies for a Third Party Review Organization should be fully implemented and there should be an attestation that those policies have been implemented that is signed by the most responsible individual at the organization before any submission is accepted for review. When using external Technical Experts, see Section V.C.(4) of this guidance for more information on conflicts of interest safeguards.

(3) Personnel involved in reviewing activities

Third Party Review Organizations and their personnel[95] should demonstrate knowledge and experience with the following, as applicable:

- The Federal Food, Drug, and Cosmetic Act;
- The Public Health Service Act; and
- Regulations in the Code of Federal Regulations implementing these statutes, particularly 21 CFR Chapter I Subchapter H.

Additionally, the Third Party Review Organization should:

- Establish, document, and execute policies and procedures to ensure that submissions are reviewed by qualified personnel.
- Maintain records on the relevant education, training, skills, and experience of all personnel who contribute to the technical review of a submission.
- Make available to its personnel clear written instructions for duties and responsibilities with respect to reviews conducted for FDA.
- Employ personnel who are qualified in all the scientific disciplines relevant to the submission that the 3P510k RO accepts for review or that the 3PEUA RO is under contract to review.

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[94] Available at: https://www.oge.gov/web/OGE.nsf/0/A8ECD9020E3E384C8525873C0046575D/$FILE/SOC%20as%20of%2085%20FR%2036715%20FINAL.pdf

[95] For additional information on the criteria for 3P510k RO personnel qualifications see Medical Devices; Implementation of Third Party Review Under the Food and Drug Administration Modernization Act of 1997; Emergency Processing Request Under OMB Review, 63 FR 28388, May 22, 1998, available at https://www.gpo.gov/fdsys/pkg/FR-1998-05-22/pdf/98-13799.pdf

- Identify at least one individual who is responsible for providing supervision over reviews and who has sufficient authority and competence to assess the quality and acceptability of these reviews.

In addressing the items enumerated above in this section, Third Party Review Organizations should be consistent with IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews,"[96] including, but not limited to, maintaining a quality management system, and IMDRF GRRP WG/N40 FINAL:2017: "Competence, Training, and Conduct Requirements for Regulatory Reviewers."[97] For more information on IMDRF GRRP, see Section V.F of this guidance below.

In addition, Third Party Review Organizations will be expected to consult national and/or international standards recognized by FDA as well as FDA guidance documents. Third Party Review Organizations should have the capability to interface with FDA's electronic data systems and websites through which the Third Party Review Organization can search for relevant guidance documents, recognized standards, predicate summaries where appropriate, and publicly available information regarding adverse events and recalls when performing review of similar devices. FDA may also provide additional guidances and templates in certain emergency situations, including as an emergency evolves (e.g., FDA published templates on its website for SARS-COV-2 tests).

3P510k ROs must certify in their application that designated personnel will attend FDA's training for recognition and rerecognition (see Section V.D.(1) of this guidance and the Federal Register notice published on May 22, 1998 (63 FR 28388)). 3P510k ROs are expected to complete training before conducting any 510(k) reviews under the program. FDA will not accept reviews and recommendations of 510(k) submissions from 3P510k ROs that have failed to have at least one designated person attend an FDA training session for recognition.

3PEUA ROs personnel are also expected to be appropriately trained. 3PEUA ROs should reference the resources available through CDRH Learn[98] to ensure personnel are familiar with the basics of FDA's regulation of medical devices and CDRH's structure prior to reviewing an EUA request. Personnel reviewing in vitro diagnostic products should complete the in vitro diagnostic product training prior to reviewing an EUA request for such product. 3PEUA ROs should also be familiar with FDA's guidance "Emergency Use Authorization of Medical Products and Related Authorities." When reviewing an EUA request that references standards, personnel should complete the relevant CDRH training on the use of standards and the Accreditation Scheme for Conformity Assessment (ASCA). Depending on the circumstances of

[96] IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews" can be found at https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-200318-rrar-cab-cmdrr-n59.pdf

[97] IMDRF GRRP WG/N40 FINAL:2017: "Competence, Training, and Conduct Requirements for Regulatory Reviewers" can be found at http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-competence-conduct-reviewers.pdf

[98] CDRH Learn is available at https://www.fda.gov/training-and-continuing-education/cdrh-learn.

an emergency, FDA may also recommend other device-specific trainings prior to 3PEUA ROs reviewing EUA requests.

3P510k ROs should be prepared to conduct technically competent 510(k) reviews before requesting recognition by FDA. FDA recommends persons reviewing 510(k) submissions review at a 3P510k RO meet the appropriate qualifications (e.g., specialized education and experience) provided in this guidance. When a 3P510k RO requests to expand the scope of device types for which they may review 510(k) submissions, it should ensure through its policies and procedures in place that its staff are qualified in the scientific disciplines for the new device types.

(4) Use of external Technical Experts

The following are FDA's recommendations when Third Party Review Organizations use an external Technical Expert:

- The Third Party Review Organization should ensure that external Technical Experts meet the same standards as those who work within the Third Party Review Organization, such as freedom from conflicts of interest;
- The Third Party Review Organization should ensure that external Technical Experts are discouraged from subcontracting parts of their contract to subcontractors, and if they do so, then the external Technical Expert should ensure that the subcontractor meets all requirements applicable to the external Technical Expert; and
- Third Party Review Organizations should maintain records of the qualifications of external Technical Experts, in addition to evidence of regular monitoring of the established competence, conflicts of interest and the degree of fulfillment of the outsourced work.

For 3P510k ROs, since they request a list of product codes to be recognized to review, they should ensure they have sufficient competence among their own staff to review the device types covered by those product codes. There should be at least one qualified Product Specialist per device type that the 3P510k RO is recognized to review. This is to ensure that there is not excessive reliance on external expertise by a 3P510k RO and to enable appropriate oversight of the qualifications of external Technical Experts by 3P510k ROs. For 3PEUA ROs, FDA may request information in the form of curricula vitae (CVs) or resumes to ensure sufficient expertise and identify key personnel in contracts.

In addressing the items above, Third Party Review Organizations should be consistent with IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews[99] and IMDRF GRRP WG/N40 FINAL:2017: "Competence, Training, and Conduct

[99] IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews" can be found at https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-200318-rrar-cab-cmdrr-n59.pdf

Requirements for Regulatory Reviewers."[100] For more information on IMDRF GRRP and MDSAP, see Section V.F of this guidance below.

(5) Confidential information

A Third Party Review Organization is required to treat information received in submissions, as well as certain information contained in records, reports, and recommendations as proprietary information (for 3P510k review, see section 523(b)(3)(F)(iii) of the FD&C Act) and may not generally publicly disclose confidential commercial information or any trade secret (for 3P510k review, see also section 301(y)(2) of the FD&C Act).[101] Also, in accordance with 21 CFR 807.95, when a 510(k) is submitted by a device manufacturer to FDA, FDA will not publicly disclose that submission if certain conditions are met. Similarly, FDA will generally not publicly disclose that an EUA request has been submitted prior to issuing an EUA authorization. Thus, a Third Party Review Organization should not publicly disclose a submission for a device that is not currently on the market and where the intent to market the device has not been disclosed.

FDA will determine whether information submitted to FDA by a Third Party Review Organization can be released in accordance with the Trade Secrets Act, Freedom of Information Act, 21 CFR part 20 and 21 CFR 807.95, regarding confidentiality of information in 510(k)s. In general, submissions submitted by Third Party Review Organizations and associated review documentation will be available for disclosure by FDA after the agency has issued an SE or authorization decision for a device, unless the information is exempt or prohibited from public disclosure under 21 CFR part 20 or 21 CFR 807.95, among other relevant authorities. FDA may seek predisclosure notification input from 510(k) and EUA submitters consistent with 21 CFR 20.61, as appropriate.

In addition, information submitted by a 3P510k RO to obtain recognition or rerecognition from FDA is available for public disclosure unless exempt or prohibited from public disclosure.

(6) Complaints regarding Submitters

The 3P510k RO should send to FDA via email to 3P510K@fda.hhs.gov information on any complaint (e.g., whistleblowing) it receives about a 510(k) Submitter that could indicate an issue related to the safety or effectiveness of a medical device or a public health risk.

A 3PEUA RO should send such a complaint about an EUA submitter via email to the contact provided in its contract with FDA.

(7) Third Party Review Organization recordkeeping

[100] IMDRF GRRP WG/N40 FINAL:2017: "Competence, Training, and Conduct Requirements for Regulatory Reviewers" can be found at http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-competence-conduct-reviewers.pdf

[101] For contracts, see section 708(a) of the FD&C Act and 21 CFR 20.90.

Pursuant to section 704(f) of the FD&C Act, a 3P510k RO must maintain records that support its initial and continuing qualifications to receive FDA recognition. These records must include the following:

- Documentation of the training and qualifications of the Third Party Review Organization and its personnel;
- The procedures used by the Third Party Review Organization for handling confidential information;
- The compensation arrangements made by the 3P510k RO; and
- The procedures used by the Third Party Review Organization to identify and avoid conflicts of interest.

3PEUA ROs would maintain records as described in the contract between FDA and the 3PEUA RO, as applicable.

In addition, FDA recommends that Third Party Review Organizations retain the following records for at least three years (3) following the submission of a submission for review to FDA:

- Copies of all submission reviews and associated correspondence;
- Information on the identity and qualifications of all personnel who contributed to the technical review of each submission; and
- Other relevant records.

In addressing the items enumerated above, Third Party Review Organizations should be consistent with IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews"[102], including records consistent with their quality management system, and IMDRF GRRP WG/N40 FINAL:2017: "Competence, Training, and Conduct Requirements for Regulatory Reviewers."[103] For more information on the IMDRF documents, see Section V.F of this guidance.

In accordance with section 704(f)(1) of the FD&C Act, 3P510k ROs must make the records specified in that section available upon request by FDA. 3P510k ROs shall permit an FDA officer or employee at all reasonable times to have access to, copy, and/or verify these records. Within 15 days of receipt of a written request from FDA, 3P510k ROs must make copies of the requested records available at the place FDA designates.[104] If FDA's monitoring of the 3P510k Review Program, such as a review of compensation arrangements between 3P510k ROs and 510(k) Submitters, reveals that 510(k) Submitters are developing business relationships with

[102] IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews" can be found at https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-200318-rrar-cab-cmdrr-n59.pdf

[103] IMDRF GRRP WG/N40 FINAL:2017: "Competence, Training, and Conduct Requirements for Regulatory Reviewers" can be found at http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-competence-conduct-reviewers.pdf

[104] See section 704(f)(2) of the FD&C Act.

3P510k ROs that call into question the independence or objectivity of a 3P510k RO, FDA will consider limiting a Submitter's choice of 3P510k ROs. Business relationships that may undermine the independence or objectivity of a 3P510k RO include, for example, contracts between a manufacturer and a 3P510k RO that represent a significant share of the 3P510k RO's income.

3PEUA ROs would make records available as described in the contract between FDA and the 3PEUA RO, as applicable.

Section 523(b)(3)(F)(iv) of the FD&C Act requires 3P510k ROs to agree that they will promptly respond and attempt to resolve complaints regarding the activities for which they are accredited. FDA recommends that 3P510k ROs establish a recordkeeping system for tracking the submission of those complaints and how those complaints were resolved, or attempted to be resolved. FDA recommends that 3PEUA ROs maintain similar records.

D. Content and Format of an Application for Initial Recognition and Rerecognition as a 3P510k Review Organization

This section of the guidance provides FDA's recommendations on what should be included in an application to FDA for recognition as a 3P510k RO.[105] The 3P510k RO should inform FDA promptly if they would like to suspend, withdraw, cancel or reduce the scope of their program. FDA will adjust recognition or rerecognition as appropriate.

(1) Initial Recognition

Organizations that wish to become recognized as 3P510k ROs under section 523 of the FD&C Act should send their applications to FDA as a single portable document format (PDF) file to:

3P510k@fda.hhs.gov
Attention: CDRH Third Party Premarket Review Program

Alternatively, applications can be sent by mail to the following address:

CDRH Third Party Premarket Review Program
U.S. Food and Drug Administration
Document Control Center (DCC) – WO66-G609
10903 New Hampshire Avenue,
Silver Spring, Maryland 20993 USA.
3P510K@fda.hhs.gov

[105] As discussed in Section II.B of this guidance, for 3PEUA ROs, FDA intends to contract with them directly based on the circumstances of an emergency, including when the Agency determines that help with review would be beneficial.

To facilitate review of the application, FDA strongly encourages submission of an eCopy.[106]

FDA will acknowledge receipt with an email to the applicant's designated contact person when the application is received. FDA will review these materials and respond within 60 calendar days[107] of the date of the receipt of the application with a decision to recognize or deny recognition, or a request for additional information. FDA may deem the application incomplete and deny recognition if the applicant fails to respond to FDA's request for additional information in a timely manner.

To facilitate review, the following information should be submitted in an application for FDA's consideration:

a. Administrative information

- The name and mailing address of the 3P510k RO seeking recognition;
- The telephone number, email address, and fax number of the contact person. The contact person should be the person to whom questions about the content of the application may be addressed and the person to whom a letter of determination and general correspondence will be directed;
- The name and title of the most responsible individual at the 3P510k RO;
- A brief description of the 3P510k RO, including: type of organization (e.g., not-for-profit institution, commercial business, other type of organization); size of organization (number of employees); number of years in operation; nature of work (e.g., testing or certification laboratory); and information regarding ownership (i.e., name of owner(s) and extent of ownership), operation, control of organization, and other related information sufficient for FDA to assess its degree of independence from entities such as device manufacturers and distributors;
- A listing of any national, state, local, or other recognition; and
- A list of the device types the applicant seeks to review by product codes or classification regulation name and regulation. Please refer to the FDA Third Party public website[108] for devices that are eligible for 3P510k review.

b. Prevention of conflicts of interest

A copy of the written policies and procedures established by the 3P510k RO to ensure that the 3P510k RO and its employees, external Technical Experts, contractors and individual contract employees involved in the evaluation of 510(k)s are free from conflicts of interest, and to prevent

[106] For information on the eCopy program, please see FDA's guidance entitled "eCopy Program for Medical Device Submissions."
[107] See section 523(b)(2)(A) of the FD&C Act.
[108] Information on third party eligible device types is available on FDA's website: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfThirdParty/current.cfm

any individual or organizational conflict of interest, or appearance of conflict of interest that might affect the review process.

c. Personnel qualifications

A list of personnel who will be involved in the preparation of the 3P510k RO's 510(k) recommendations, including Product Specialists, Technical Experts, external Technical Experts, and Final Reviewers. Applicants should demonstrate that these personnel are technically competent to conduct 510(k) reviews and should document the following in their application:

- The written policies and procedures established to ensure 510(k)s are reviewed by qualified personnel;
- The written instructions for the duties and responsibilities of personnel with respect to 510(k) reviews;
- The written personnel standards established to ensure that designated personnel are qualified in all of the scientific disciplines presented by the 510(k)s for devices for which the 3P510k RO is applying for its review;
- The documentation (e.g., CVs) to establish that the reviewers of 510(k)s (i.e., Product Specialists and Technical Experts) and other involved non-supervisory personnel meet the Recognition Criteria for qualified personnel. This includes documentation of education, training, skills, abilities, and experience, including specialized education and experience needed for the review of devices for which the 3P510k RO is applying for its review;
- The documentation (e.g., CVs) to establish that the supervisor(s) of 510(k) reviewers (i.e., Final Reviewer) have sufficient authority and meet the Recognition Criteria for qualified supervisory personnel. This includes documentation of education, training, skills, abilities, and experience, including specialized education and experience needed for the review of class II devices for which the 3P510k RO is applying for its review; and
- A description of the management structure, or, if an external technical expert is used for 510(k) reviews, the external Technical Expert's management structure. The application should describe the position of the individual(s) providing supervision within the management structure and explain how that structure provides for the supervision of 510(k) reviewers and other personnel involved in the review process.

Throughout the period of recognition, a 3P510k RO should ensure its personnel remain technically competent and only conduct 510(k) reviews for which they have the technical competency to do the review. If a 3P510k RO does not continue to demonstrate its personnel remain technically competent and only conduct 510(k) reviews for which they have technical competency to do the review, FDA may take action at any time to ensure that the 3P510k RO is only reviewing 510(k) submissions for which it has the technical competency to review.

d. Certification statements

As required by statute, and to support FDA's plan to eliminate routine re-review of 3P510(k) submissions,[109] the applicant must provide a statement in their application, signed by the most responsible individual at the organization, certifying that the 3P510k RO has committed at the time of accreditation and at any time it is performing any 3P510k review that it:

- Will report information that accurately reflects data reviewed;
- Will limit work and reviews to that for which competence and capacity are available, including conducting 510(k) reviews in accordance with the policies and procedures it has established regarding review of 510(k)s by qualified personnel;
- Will treat any information, records, reports, and recommendations that it may receives as proprietary and confidential information;
- Will promptly respond and attempt to resolve complaints regarding the activities for which it is recognized;
- Will protect against conflicts of interests in accordance with policies and procedures it has established relating to prevention of financial conflicts of interests, and annually make available to the public disclosures of the extent to which the person, and the officers and employees of the person, have maintained compliance with requirements relating to financial conflicts of interest;

FDA also encourages the applicant to certify in its application that at all times, it:

- Will demonstrate conformity while recognized by FDA with the requirements of section 523 of the FD&C Act;
- Will maintain records in a manner consistent with Section V.C.(7) of this guidance;
- Will comply with the eCopy requirements for premarket submissions as described in the guidance document entitled, "eCopy Program for Medical Device Submissions;"
- Commits that its most responsible person or designee(s) will have completed FDA training prior to performing any reviews by the 3P510k RO, and agrees that its most responsible person or designee(s) will attend such training when offered and applicable;
- Will contact FDA for EI before reviewing any subset of device type (by respective product code) that it has not reviewed as encouraged in Section V.B.(4) of this guidance; and
- Will commit to only accepting reviews where the 510(k) Submitters certified that any relevant prior communications with FDA are disclosed.

(2) Rerecognition

In accordance with section 523(b)(2)(D) of the FD&C Act, a 3P510k RO's recognition by FDA will sunset 3 years from the date the recognition was granted. To continue conducting 3P510k reviews beyond 3 years from the date of the last recognition or rerecognition, the 3P510k RO

[109] See Eliminating Routine FDA Re-Review of Third Party 510(k) Reviews, available at https://www.fda.gov/media/116168/download

must obtain rerecognition. 3P510k ROs should apply for rerecognition a minimum of 60 calendar days before their recognition status expires to prevent any lapse in recognition. A 3P510k RO may request a rerecognition earlier if it so chooses.

Requests for rerecognition will be handled in the same manner as initial recognition requests. Accordingly, rerecognition applications should follow the format described in Section V.C.(1) of this guidance. For rerecognition, FDA may also consider the past premarket review performance of the 3P510k RO and any information that comes to FDA's attention about the status of the 3P510k RO's recognition, including information from an audit.[110] Through rerecognition, FDA may also modify the product codes which personnel are reaccredited to review.[111]

(3) Recognition or Rerecognition Denial

A 3P510k RO that wishes to request a reconsideration of a recognition denial or rerecognition denial should appeal under 21 CFR 10.75 as a request for supervisory review following the appeals process outlined in FDA's guidance entitled "Center for Devices and Radiological Health Appeals Processes."[112]

E. Suspension or Recognition Withdrawal

Section 523(b)(2)(B) of the FD&C Act authorizes FDA to suspend or withdraw recognition of any 3P510k RO, after providing notice and an opportunity for an informal hearing, when the 3P510k RO is substantially not in compliance with the requirements of section 523 of the FD&C Act, poses a threat to public health, or fails to act in a manner that is consistent with the purposes of section 523.

Under section 301(y)(1) of the FD&C Act, the following actions are prohibited by a 3P510k RO:

- Submission of a report or recommendation that is false or misleading in any material respect;
- Disclosure of confidential information or any trade secrets without the express written consent of the person who submitted such information or secrets to the 3P510k RO; and
- Receipt of a bribe in any form or doing any corrupt act associated with a responsibility delegated to the 3P510k RO under the FD&C Act.

In general, 3PEUA ROs should also refrain from the above activities substituting 3PEUA RO for 3P510(k) RO in the last two bullets and look to the contract between FDA and the 3PEUA RO for specific requirements.

[110] See section 523(b)(2)(C) of the FD&C Act.
[111] See section 523(b)(2)(D)(iii) of the FD&C Act.
[112] See also the guidance "Center for Devices and Radiological Health (CDRH) Appeals Processes: Questions and Answers About 517A."

Furthermore, FDA intends to periodically evaluate completed premarket reviews of 510(k)s and authorized EUAs submitted to FDA under the 3P510k Review Program or reviewed by a 3PEUA RO and intends to provide feedback to Product Specialists and the Final Reviewer following evaluation.

FDA intends to perform an assessment of each 3P510k RO on a periodic (at least once every three years)[113] or "for cause" basis as part of its auditing to ensure 3P510k ROs continue to meet the standards of recognition (see section 523(b)(2)(C) of the FD&C Act). As resources allow, assessments will involve inspecting a 3P510k RO's facility and/or records to ensure that the 3P510k RO is operating in accordance with the procedures, qualifications, and certifications specified in the 3P510k RO's application and the FD&C Act.

3P510k ROs should continue to demonstrate technical competency to maintain recognition. If monitoring of a 3P510k RO reveals nonconformity with section 523 of the FD&C Act, a threat to the public health, or a failure to act in a manner that is consistent with the purposes of section 523, FDA may take steps to suspend or withdraw recognition of the 3P510k RO, after providing notice and an opportunity for an informal hearing.[114]

F. Leveraging the International Medical Device Regulators Forum's (IMDRF's) documents

In February 2011, the IMDRF was convened to discuss future directions in medical device regulatory harmonization. The IMDRF is a voluntary group of medical device regulators from around the world, including representatives from the FDA, who collaborate to build on the strong foundational work of the Global Harmonization Task Force on Medical Devices. The purpose of the IMDRF is to accelerate international medical device regulatory convergence.

The IMDRF Good Regulatory Review Practices (GRRP) working groups developed documents that provide the fundamental building blocks of third party review that can be applicable to submissions such as 510(k) submissions and EUA requests by providing criteria for reviewer competence, training, and conduct, and, for organizations, the expectations for entities ("Conformity Assessment Bodies" or CABs) that perform regulatory reviews. Details are outlined in a collection of documents finalized from 2017 through 2023 and available on the IMDRF website.[115]

[113] See section 523(b)(2)(D)(i) of the FD&C Act.

[114] See section 523(b)(2)(B) of the FD&C Act.

[115] The IMDRF published eight documents related to GRRP. All the IMDRF documents are available on the IMDRF website at: https://www.imdrf.org/working-groups/good-regulatory-review-practices. This guidance references IMDRF GRRP WG N40 Final:2017, "Competence, Training, and Conduct Requirements for Regulatory Reviewers," IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews," and IMDRF GRRP WG N66 "Assessment and Decision Process for the Recognition of a Conformity Assessment Body Conducting Medical Device Regulatory Reviews.

There are many shared elements in FDA's statutory and regulatory criteria for Third Party Review Organizations and IMDRF GRRP WG N40 FINAL:2017: "Competence, Training, and Conduct Requirements for Regulatory Reviewers," [116] IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews." [117] These documents focus on expectations for CABs and the individuals CABs engage to perform regulatory reviews and other related functions under the respective medical device legislation, regulations, and procedures required in its regulatory jurisdiction.

Due to these similarities, FDA believes that potential Third Party Review Organizations in compliance with the GRRP documents cited, as appropriate, are likely to be in alignment with most FDA 3P510k RO requirements and 3PEUA RO recommendations outlined in this guidance document. Such organizations do not necessarily need to generate new documentation for FDA, but rather can leverage existing documents in their applications to FDA and for ongoing recordkeeping.

[116] IMDRF/GRRP WG/N40 FINAL:2017: "Competence, Training, and Conduct Requirements for Regulatory Reviewers," previously cited, can be found at http://www.imdrf.org/docs/imdrf/final/technical/imdrf-tech-170316-competence-conduct-reviewers.pdf

[117] IMDRF GRRP WG N59 Final:2020 "Requirements for Regulatory Authority Recognition of Conformity Assessment Bodies Conducting Medical Device Regulatory Reviews" can be found at https://www.imdrf.org/sites/default/files/docs/imdrf/final/technical/imdrf-tech-200318-rrar-cab-cmdrr-n59.pdf