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# **Investigational In Vitro Diagnostics in Oncology Trials: Streamlined Submission Process for Study Risk Determination Guidance for Industry**

## ***DRAFT GUIDANCE***

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For questions regarding this draft document, contact (CDER) Julie Schneider at 240-402-4658; (CDRH) Yun-Fu Hu at 301-796-6170; or (CBER) Stephen Ripley at 240-402-7911.

**U.S. Department of Health and Human Services  
Food and Drug Administration  
Oncology Center of Excellence  
Center for Drug Evaluation and Research (CDER)  
Center for Biologics Evaluation and Research (CBER)  
Center for Devices and Radiological Health (CDRH)**

**April 2018  
Procedural**

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1                   **Investigational In Vitro Diagnostics in Oncology Trials:**  
2                   **Streamlined Submission Process**  
3                   **for Study Risk Determination**  
4                   **Guidance for Industry<sup>1</sup>**  
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6

7  
8 This draft guidance, when finalized, will represent the current thinking of the Food and Drug  
9 Administration (FDA or Agency) on this topic. It does not establish any rights for any person and is not  
10 binding on FDA or the public. You can use an alternative approach if it satisfies the requirements of the  
11 applicable statutes and regulations. To discuss an alternative approach, contact the FDA staff responsible  
12 for this guidance as listed on the title page.  
13

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15  
16 **I. INTRODUCTION AND BACKGROUND**  
17

18 The purpose of this guidance is to describe an optional streamlined submission process for  
19 determining whether use of an investigational in vitro diagnostic (IVD) in a clinical trial for an  
20 oncology therapeutic is considered significant risk (SR), nonsignificant risk (NSR), or exempt.<sup>2</sup>  
21 If found to be SR, such a trial may require approval of an investigational device exemption (IDE)  
22 in addition to an investigational new drug application (IND). FDA encourages sponsors to use  
23 the streamlined process described in this guidance when possible to reduce administrative burden  
24 on sponsors and FDA and to maintain the current level of regulatory review.  
25

26 Regardless of whether a study involving an investigational IVD is determined to be SR or NSR,  
27 it must follow the abbreviated requirements outlined in 21 CFR 812.2(b),<sup>3</sup> including generating  
28 and retaining data that demonstrate analytical validation of the investigational IVD. Sponsors can  
29 contact CDRH directly with questions relating to analytical validation of the investigational IVD.  
30

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

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<sup>1</sup> This guidance has been prepared by the Oncology Center of Excellence, Center for Drug Evaluation and Research, Center for Biologics Evaluation and Research, and Center for Devices and Radiological Health (CDRH) at the Food and Drug Administration.

<sup>2</sup> 21 CFR 812.2(c)

<sup>3</sup> For more information about the abbreviated requirements for NSR devices, see the guidance for industry and FDA staff *In Vitro Diagnostic (IVD) Device Studies — Frequently Asked Questions*. This guidance is available on the FDA Medical Devices and Radiation Emitting Products guidance web page at <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm>.

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

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### **II. APPLICABILITY OF THE STREAMLINED SUBMISSION PROCESS**

- The streamlined submission process described in this guidance applies only to clinical trials involving codevelopment of an investigational IVD with an oncology investigational drug. It does not apply to codevelopment programs in other disease areas.
- Sponsors can continue to submit requests for risk determinations for investigational IVDs in oncology codevelopment studies using the Q-submission program.<sup>4</sup>
- The streamlined submission process described in this guidance does not apply to IND-exempt studies.
- If an invasive biopsy that presents a potential for serious risk to the health, safety, or welfare of the subject is required for investigational IVD testing for enrollment,<sup>5</sup> the study is not eligible for the streamlined submission process. If a sponsor submits such a study via the streamlined process, FDA will notify the sponsor to consult with CDRH for a study risk determination through the Q-submission program.

### **III. DESCRIPTION OF THE STREAMLINED SUBMISSION PROCESS**

The sponsor should submit all information about the oncology codevelopment program (including information about the investigational IVD) to the appropriate center (CBER or CDER) for the IND. As part of the IND review, CBER or CDER will consult CDRH and determine if the investigational IVD is SR, NSR or exempt. The sponsor should consider the following for the submission:

- One sponsor should take the lead in communicating with FDA about the IND. FDA intends to communicate all feedback (including feedback about the investigational IVD) to the same lead sponsor.
- The list below highlights how a sponsor should present information in the IND submission to facilitate the streamlined submission process, when applicable:
  - In FDA form 1571 (in section 11 under “Other”), sponsors should indicate the intent to utilize the streamlined submission process. A sponsor also can include this

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<sup>4</sup> For more information about study risk determination through the Q-submission program in CDRH, see the guidance for industry and FDA administration staff *Requests for Feedback on Medical Device Submissions: The Pre-Submission Program and Meetings with Food and Drug Administration Staff*. This guidance is available on the FDA Medical Devices and Radiation-Emitting Products guidance web page at <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm>.

<sup>5</sup> See 21 CFR 812.3(m).

## ***Contains Nonbinding Recommendations***

*Draft — Not for Implementation*

- 75 information in a cover letter if the sponsor intends to submit a cover letter with the  
76 IND.  
77
- 78 – In the protocol,<sup>6</sup> a sponsor should include information about:  
79
- 80 • How the results from the investigational IVD will be applied in the clinical  
81 trial  
82
  - 83 • What is known about the prevalence of the biomarker (evaluated by the  
84 investigational IVD) in the patient population; and  
85
  - 86 • The specimen type that will be collected for investigational IVD testing  
87 (including the anatomical site) and whether any biopsy required for  
88 investigational IVD testing could present a potential for serious risk to the  
89 health, safety, or welfare of the subject.<sup>7</sup>  
90
- 91 – By signing FDA form 1571 (section 17) sponsors provide assurance of an  
92 institutional review board (IRB) review for the investigational IVD and the  
93 investigational drug.<sup>8</sup> FDA recommends that informed consent documents reviewed  
94 by the IRB address risks associated with the consequences of an incorrect test result  
95 from the investigational IVD during the screening phase as well as risks associated  
96 with the investigational drug.  
97
- 98 • CBER or CDER will consult with CDRH and determine if the use of the investigational  
99 IVD in the study is SR, NSR or exempt. If the investigational IVD is NSR, CBER or  
100 CDER will confirm the NSR determination in the May Proceed Letter, which may also  
101 include a statement such as “You should ensure that NSR procedures are used in  
102 obtaining any biopsies taken for testing with the investigational IVD and submit  
103 unanticipated adverse device effect reports to the IND.” If the investigational IVD is SR,  
104 CBER or CDER will confirm the SR determination in the May Proceed Letter and may  
105 ask the sponsor to submit an IDE to CDRH and to wait to initiate the trial until after the  
106 IDE is approved.  
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<sup>6</sup> 21 CFR 312.23.

<sup>7</sup> 21 CFR 812.3(m).

<sup>8</sup> See 21 CFR 312.66 for investigational drugs and 21 CFR 812.62 for investigational IVDs.

**GLOSSARY**

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**Investigational in vitro diagnostic (IVD)**

An IVD that is the object of a clinical investigation. An investigational IVD could be a prototype clinical trial assay, a new IVD that has not previously been cleared or approved, or an IVD used in a clinical investigation for purposes other than for its cleared or approved intended use(s) or indication(s). See 21 CFR 809.3(a) for the complete definition of in vitro diagnostic product, 21 CFR 812.3(g) for the complete definition of an investigational device, and 21 CFR 812.3(h) for the definition of investigation.

**Investigational device exemption (21 CFR 812)**

An exemption that permits a sponsor to lawfully ship a device that otherwise would be required to comply with a performance standard or to have premarket approval. The exemption is for the purpose of conducting investigations of that device.

**Investigational new drug (21 CFR 312.3)**

A new drug or biological product used in a clinical investigation. The term also refers to a biological product that is also an in vitro diagnostic used in a clinical investigation.

**Nonsignificant risk device**

A device that does not meet the definition of a significant risk device (see below and 21 CFR 812.3(m)).<sup>1</sup>

**Significant risk device**

Under 21 CFR 812.3(m), a significant risk device means an investigational device that:

1. Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
2. Is purported or represented to be for a use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
3. Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
4. Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

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<sup>1</sup> For more information about nonsignificant risk studies, see the information sheet guidance for IRBs, clinical investigators, and sponsors *Significant Risk and Nonsignificant Risk Medical Device Studies*. This guidance is available on the FDA Medical Devices and Radiation-Emitting Products guidance web page at <https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/default.htm>.