Companion Diagnostics and Oncology Diagnostics Pilot Program: A CDRH Perspective

Brittany Schuck, PhD

Deputy Office Director, OHT7: Office of In Vitro Diagnostics

Center for Devices and Radiological Health

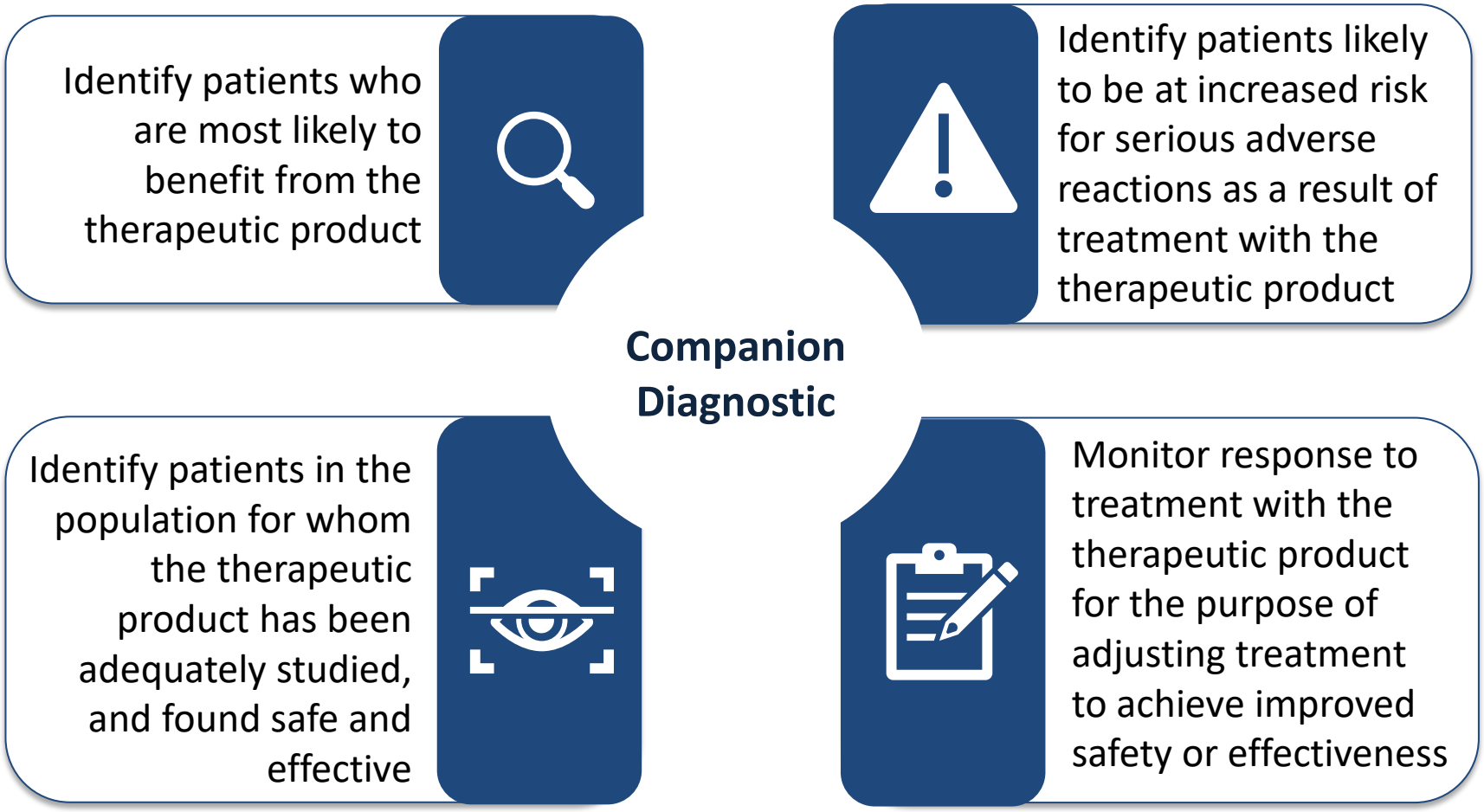
Food and Drug Administration

Outline

- Companion diagnostics policy
- New voluntary pilot program for certain oncology drugs
- Looking forward

Companion Diagnostics

An in vitro diagnostic (IVD) that provides information that is essential for the safe and effective use of a corresponding therapeutic product



Companion Diagnostics (CDx)

The FDA issued final guidance "In Vitro Companion Diagnostic Devices", August 2014

Ideally, a therapeutic product and its corresponding CDx should be developed and authorized contemporaneously

- The clinical performance and clinical significance of the companion diagnostic should be established using data from the clinical development program of the corresponding therapeutic product

The use of a CDx with a therapeutic product is stipulated in the instructions for use in the labeling of both the diagnostic device and the corresponding therapeutic product

FDA applies a risk-based approach to determine the regulatory pathway for CDxs, as it does with all medical devices

Current CDx Program

As of 08/15/2023, FDA has approved or cleared **more than 50 companion diagnostics**, encompassing **more than 130 indications**

Highlights

In 2023, FDA approved the first companion diagnostic test intended to help health care providers identify patients who may benefit from treatment with a gene therapy.

In 2022, FDA approved two new tumor agnostic companion diagnostic indications, including the first tumor agnostic next-generation sequencing companion diagnostic for the detection of Microsatellite Instability High status in patients with solid tumors

Current Environment

- As described in FDA's CDx guidance[1], there are specific circumstances where FDA may decide to approve a drug without clearing, approving, or authorizing a corresponding CDx at the same time.

> ***1. New Therapeutic Products to Treat Serious or Life-Threatening Conditions***
>
> FDA may decide to approve a therapeutic product even if an IVD companion diagnostic device is not yet approved or cleared when the therapeutic product is intended to treat a serious or life-threatening condition for which no satisfactory alternative treatment exists and the benefits from the use of the therapeutic product are so pronounced as to outweigh the risks from the lack of an approved or cleared IVD companion diagnostic device. This will be determined by FDA during product review.

- In these cases, tests offered as laboratory-developed tests (LDTs)[2] with unknown performance are being used for patient treatment decisions.
- Historically, FDA has generally exercised enforcement discretion with respect to most LDTs, meaning that, except in certain circumstances, FDA generally does not exercise its authority to enforce the regulatory requirements for these devices, although it maintains that authority.

[1] https://www.fda.gov/media/81309/download

[2] For the purposes of FDA's guidance "Oncology Drug Products Use with Certain In Vitro Diagnostic Tests: Pilot Program", the term laboratory developed test (LDT) means an in vitro diagnostic device that is intended for clinical use and designed, manufactured and used within a single laboratory certified under the Clinical Laboratory Improvement Amendments (CLIA) (42 U.S.C. 263a) that meets the requirements to perform tests of high complexity, as described in 42 CFR 493.17(c)(4) and 493.25, and is a location that has its own CLIA certificate as described in 42 CFR 493.43(a).

Current Environment

FDA is concerned that LDTs used to identify patient biomarkers may not be accurate or reliable

FDA is particularly concerned that LDTs used to identify patients for drug treatment when there is not an FDA authorized companion diagnostic may not perform well

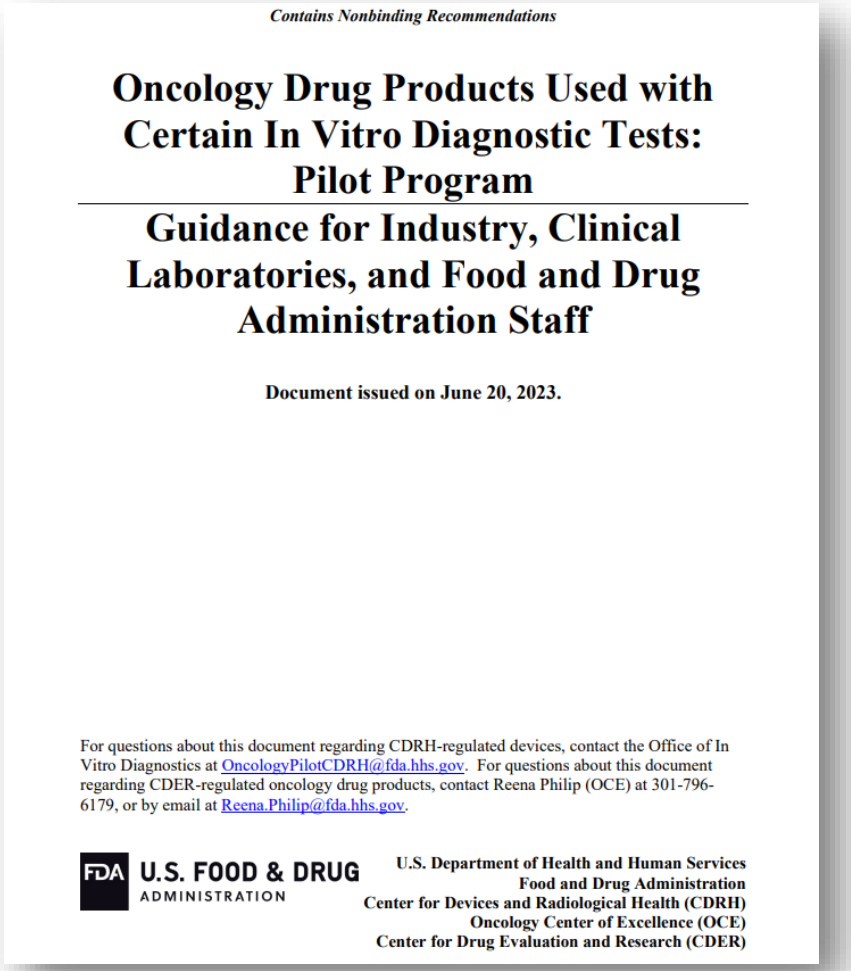
Recommend minimum performance characteristics for tests used to identify patients for certain oncology drugs to address safety risks posed by LDTs

Oncology Drug Products Used with Certain In Vitro Diagnostic Tests: Pilot Program

FDA is piloting a new approach to provide greater transparency regarding minimum performance characteristics that certain tests for certain oncology drugs should meet

- One step that may be helpful in reducing the risk of using LDTs for oncology drug treatment decisions while we continue to work on a broader approach for LDTs, including **moving forward with rulemaking.**

- This pilot **does not alter the standards** for approval of the oncology drug products or for marketing authorization of the corresponding companion in vitro diagnostics.



Contains Nonbinding Recommendations

Oncology Drug Products Used with Certain In Vitro Diagnostic Tests: Pilot Program

Guidance for Industry, Clinical Laboratories, and Food and Drug Administration Staff

Document issued on June 20, 2023.

For questions about this document regarding CDRH-regulated devices, contact the Office of In Vitro Diagnostics at OncologyPilotCDRH@fda.hhs.gov. For questions about this document regarding CDER-regulated oncology drug products, contact Reena Philip (OCE) at 301-796-6179, or by email at Reena.Philip@fda.hhs.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION

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

The pilot program is limited to certain scenarios

The scope of this voluntary pilot program is limited to 9 drug sponsors and:

CDER-regulated oncology drug products for which FDA determines that:	CDRH-regulated corresponding clinical trial assay(s):
☑ use of an in vitro diagnostic test is needed to identify the intended patient population,	☑ for which there is a well-validated reference method, well-validated comparator method, and/or well-characterized materials that can be used to support test accuracy
☑ no satisfactory alternative treatment exists, and	☑ that use the same technology as a previously FDA-authorized CDx
☑ the anticipated benefits from the use of the drug product are so pronounced as to outweigh the anticipated risks from approval of the drug product without an FDA-authorized companion diagnostic	

Pilot Program

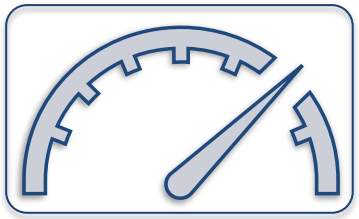
FDA

FDA intends to rely on the same pivotal clinical trial(s) that support approval of the drug product to establish the clinical validity for the clinical trial assays (CTAs) used in those trial(s).

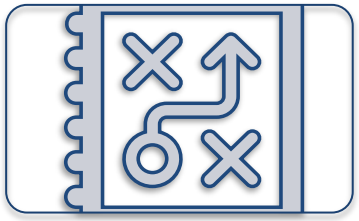
Given the type of tests eligible for use in the pilot program, FDA believes that, in general, the clinical validity of these CTAs can be extrapolated to additional tests of the same type with similar analytical performance, when established through properly conducted validation studies.

Pilot Program

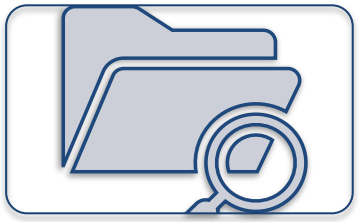
FDA will request performance information for the tests used to enroll patients into the clinical trials that support drug approval



FDA will post to its website the minimum performance characteristics recommended for similar tests that may be used to select patients for treatment with the approved drug



Laboratories may use this information to guide their development of LDTs to identify specific biomarkers used for selecting cancer treatment



This transparency aims to help facilitate better and more consistent performance of these tests, resulting in better drug selection and improved care for patients with cancer

Pilot Program: Templates

CDRH's website includes a series of templates that oncology drug product sponsors may use to facilitate the provision of performance characteristic and validation information for CTAs used in the drug product pivotal clinical trial(s), **when requested by FDA**

Templates for Collecting and Providing Performance Characteristics and Validation Information for Clinical Trial Assays:

- Next generation sequencing test template
- Polymerase chain reaction test template
- Sanger sequencing test template
- Immunohistochemistry test template
- Fluorescence in situ hybridization test template

Pilot Program: Procedures

Oncology drug pivotal trial(s) **have not started** as of June 23, 2023	• FDA will provide minimum validation and performance characteristics for CTAs to enroll the drug product's pivotal clinical trial(s), prior to the start of the trial • FDA expects the CTAs for trial enrollment will meet or exceed these validation and performance characteristics • If the drug is approved, FDA will recommend minimum performance characteristics for IVDs to be used with that drug based upon performance of the CTAs used in the clinical trials
Oncology drug pivotal trial(s) **were initiated prior** to June 23, 2023	FDA will work with drug sponsors accepted into pilot to review the performance characteristic and validation information for each CTA and recommend the minimum performance characteristics within the NDA/BLA application review timeframe

Key Takeaways

FDA believes transparency regarding **minimum recommended performance characteristics** will help facilitate development of better and more consistently performing tests, resulting in better drug selection and improved care for patients with cancer

However, this pilot program **will not** assure that LDTs available to patients are accurate and reliable

Separately, FDA issued a proposed rule regarding LDTs

Looking Forward

This pilot program may facilitate regulatory submissions to FDA

- Conventional manufacturers are still required to obtain FDA marketing authorization, which is typically sought through the PMA pathway for companion diagnostics.
- Minimum performance characteristics may be leveraged to support premarket application (PMA) approval or the development of special controls.
  - Help open the de novo pathway, and subsequently the 510(k) pathway, if the statutory criteria for the de novo pathway are met.
  - Availability of de novo and 510(k) pathways may incentivize voluntary submissions for LDTs.

Looking Forward

Community recommendations for performance specifications

Standardization and harmonization

Development of reference materials and methods to support extrapolating clinical validity from clinical trial assays (CTAs) to other tests of the same type with similar analytical performance

Resources

- Webpages
  - Companion Diagnostics
  - Oncology Drug Products Used with Certain In Vitro Diagnostics Pilot Program
  - List of Cleared or Approved Companion Diagnostic Devices

- Guidances
  - In Vitro Companion Diagnostic Devices
  - Oncology Drug Products Used with Certain In Vitro Diagnostic Tests: Pilot Program

Brittany.Schuck@fda.hhs.gov
OncologyPilotCDRH@fda.hhs.gov