Developing and Labeling *In vitro* Companion Diagnostic Devices for a Specific Group or Class of Oncology Therapeutic Products

Draft Guidance

AMDM 2019 IVD Focus Meeting

Reena Philip, PhD.
Director
Division of Molecular Genetics and Pathology (DMPG)
Office of In Vitro Diagnostics and Radiological Health (OIR)
Center for Devices and Radiological Health (CDRH)

Disclaimer

No financial relationships to disclose

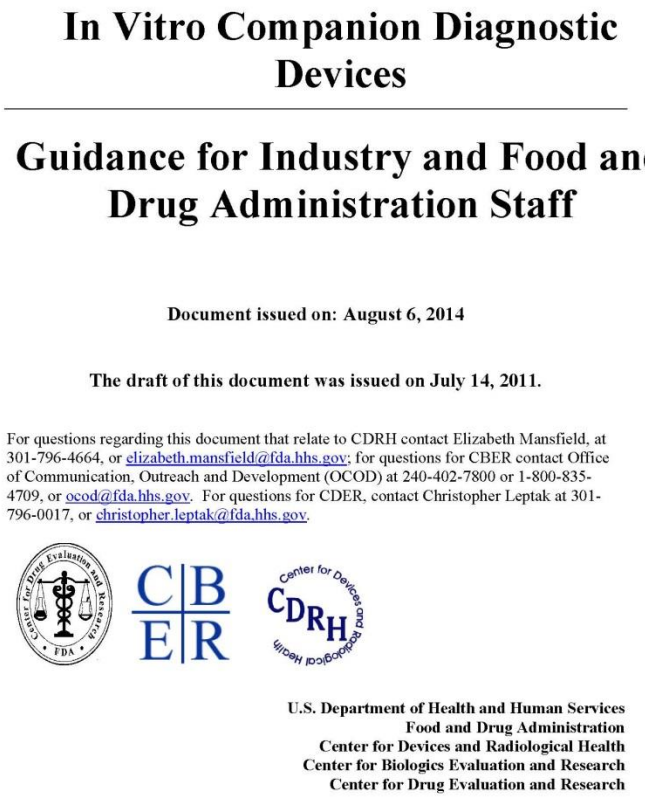
Thoughts on new regulatory issues and policies are preliminary and do not represent finalized FDA policy

Challenge

FDA approved CDx labeled for identifying NSCLC patients whose tumors have EGFR exon 19 deletions or exon 21 substitution mutations

FDA Approved CDx	**Therapeutic Products included on CDx Label**				
	Afatinib	Gefitinib	Erlotinib	Osimertinib	Dacomitinib
Therascreen EGFR RGQ PCR Kit	X	X	-	-	X
Cobas EGFR Mutation Test V2	-	-	X	X	-
Oncomine Dx Target Test	-	X	-	-	-
Foundationone CDx	X	X	X	-	-

Expands on a concept introduced in previous guidance



In Vitro Companion Diagnostic Devices

Guidance for Industry and Food and Drug Administration Staff

Document issued on: August 6, 2014

The draft of this document was issued on July 14, 2011.

For questions regarding this document that relate to CDRH contact Elizabeth Mansfield, at 301-796-4664, or elizabeth.mansfield@fda.hhs.gov; for questions for CBER contact Office of Communication, Outreach and Development (OCOD) at 240-402-7800 or 1-800-835-4709, or ocod@fda.hhs.gov. For questions for CDER, contact Christopher Leptak at 301-796-0017, or christopher.leptak@fda.hhs.gov.

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

- In some cases, if evidence is sufficient to conclude that the IVD companion diagnostic device is appropriate for use with a class of therapeutic products, **the intended use/indications for use should name the therapeutic class rather than each specific product in the class**

Proposed new EGFR CDx labelling

- *"identifying patients with NSCLC whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations and are suitable for treatment with a tyrosine kinase inhibitor approved by FDA for that indication."*

Starting point definition for a potential group or class of therapeutic products

- Potential group or class of therapeutic products must be approved for use
  - in the ***same or similar indications***
  - the ***same disease***
  - including the ***same mutation(s)*** and detected by tests using the ***same specimen type***

Considerations for implementing broader labelling

1. **The ability to define a specific group/class of therapeutic products and the companion diagnostic to identify an appropriate patient population**.
   - *Example challenge:* evolving definition of WT RAS mutations
2. **A detailed understanding of the mechanism of action of the specific group/class of therapeutic product and the interaction with the mutation**.
   - *Example challenge:* exon 19 deletions and certain exon 20 substitution mutations are known to upregulate tyrosine kinase based on functional studies but other exon 20 mutations are TKI resistant (e.g., EGFR T790M).

Considerations cont.

3. **Sufficient and consistent clinical experience with therapeutic products in the class/group** (generally with at least two FDA-approved therapeutic products)
   - *Example challenge:* it would not currently be appropriate to define a class that only targets resistant mutations (e.g., EGFR T790M and C797S)
4. **Demonstrated analytical validity of the companion diagnostic** across the range of mutations that inform the indication.
   - *Example challenge:* some mutations (e.g., fusions, CNVs rearrangements) are technically challenging to detect

Considerations cont.

5. **Demonstrated clinical validity of the companion diagnostic** through either a clinical study establishing the link between the result of the companion diagnostic and patient outcomes or clinical concordance studies with a previously approved companion diagnostic.

Class label for the following tests for identifying patients with NSCLC whose tumors have EGFR exon 19 deletions or exon 21 (L858R) substitution mutations and for treatment with a tyrosine kinase inhibitor approved by FDA for that indication

FDA Approved CDx	**Therapeutic Products included on CDx Label**				
	Afatinib	Gefitinib	Erlotinib	Osimertinib	Dacomitinib
Therascreen EGFR RGQ PCR Kit	X	X	-	-	X
Cobas EGFR Mutation Test V2	-	-	X	X	-
Oncomine Dx Target Test	-	X	-	-	-
Foundationone CDx	X	X	X	-	-

Resources

FDA website on companion diagnostics:
http://www.fda.gov/companiondiagnostics

FDA companion diagnostic guidance:
http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM262327.pdf

Developing and Labeling In vitro Companion Diagnostic Devices for a Specific Group or Class of Oncology Therapeutic Products / Guidance for Industry (Draft Guidance)

https://www.fda.gov/ucm/groups/fdagov-public/@fdagov-afdagen/documents/document/ucm627805.pdf

Thank You!

Questions?

Reena.philip@fda.hhs.gov


FDA
U.S. FOOD & DRUG
ADMINISTRATION