A Review of Codevelopment and Companion Dx Policy

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Overview

- History
- Development of policy
- The policy
- The process
- Looking forward

History of Companion Dx

- Prior to formal policy
  - ER/PR to direct therapy?
    - Not approved with a specific drug
  - Her-2/Herceptin
  - c-Kit, EGFR IHC, etc with respective drugs
- Dawning recognition that tests can be drivers of therapy

History of Companion Dx

- Policy creation
  - Change in drug development strategies to account for genetic information
  - PGx, VXDS discussions
  - Drug approvals without explicit direction to test
- Policy needed
  - Patient safety
  - Predictability—plan for device element
  - Support for therapeutic approvals

Development of Policy

- Companion Dx are *tests*
  - Need to know something about the test to understand the drug safety/effectiveness
  - Tests for the same analyte differ
    - Technology
    - Cut-off
    - Performance
  - Different tests are likely to identify different populations
- Test performance critical to *drug* performance
  - Approval, real-world use

Critical Policy Elements

- Without knowledge of the test performance:
  - drug review is compromised
  - drug cannot be adequately labeled
- Companion Dx policy rests on drug approval process

Companion Dx Policy

- Draft Guidance for Industry and Food and Drug Administration Staff - In Vitro Companion Diagnostic Devices—July 2011
  - 90 day comment period

Points of Policy (1)

- Defines “Companion diagnostic device”
  - An *IVD companion diagnostic device* is an in vitro diagnostic device that provides information that is essential for the safe and effective use of a corresponding therapeutic product.
  - Limited scope, several scenarios provided
- Why: Need to differentiate companion Dx from other Dx used for other purposes

Points of Policy (2)

- Contemporaneous approval of therapeutic and companion Dx
  - No preference for manufacturer; sponsors determine which test will be submitted for approval
- Why: Products depend on each other, need both at the same time
  - Escape hatch: benefit/risk determination when therapy is for serious or life-threatening disease with no alternative treatment
    - Device would be approved ASAP after therapy

Points of Policy (3)

- Labeling of *therapeutic product* points to "a type of approved or cleared IVD companion diagnostic device"
  - In general, specific test name will not be included, although test used in trials may be mentioned in certain sections
  - *Not limited to a single test*: "This will facilitate the development and use of more than one approved or cleared IVD companion diagnostic device of the type described in the labeling for the therapeutic product."
  - *Not a combination product* (possible rare exceptions)
- Why: Specific test design/performance will define population or dose.

Points of Policy (4)

- Labeling of *IVD companion diagnostic device* names specific drug
- Why: Need to know which test to use, performance characteristics of test usually derived from therapeutic trial

Points of Policy (5)

- Use of a test in a therapeutic trial is often *investigational*
  - Risk of use must be determined
  - Significant risk requires submission to FDA
  - *Not* dependent on who manufactures test, or whether test is already in use
- Why: IVD development is often exempt from investigational regulations; when used in therapeutic trials, it may not be

Why, why, why….

- Why wasn't CF test a companion Dx for Kalydeco?
  - CF test is part of diagnosis. Patients not retested for trial.
- Why didn't FDA require approval of test for Maraviroc or lapatinib?
  - Companion Dx policy not yet in existence, no clear understanding of FDA position
- Why isn't the guidance finalized yet?
  - That's a good question

The Codevelopment Process

- FDA has reviewed [a lot of] therapeutic development programs with potential companion Dx
- FDA has reviewed >15 companion Dx applications
- No two programs or products are exactly alike
  - Preference, timing issues, disease state, intended use, etc.
- Codevelopment guidance needed, but very hard to write
  - Mostly drafted, covers a lot of ground

Codevelopment Guidance

- Guidance will:
  - describe points to consider in both therapeutic and diagnostic development programs
  - describe FDA preferences for certain elements
  - not prescribe any particular development pathway

Looking Forward

- New issues to consider:
  - NGS as a companion Dx
    - Good idea; needs work and discussion with potential sponsors
  - Follow-on tests
    - What will be required?
    - How will FDA account for new information?
  - Tests to refine already-approved therapies
    - What will be required?
    - How does therapeutic label change work?
  - Diagnostics other than IVDs?
    - Same model should apply
    - When a specific test is needed to assess therapeutic,

Review

- Companion diagnostic policy arose out of need to assure therapeutic product safety and effectiveness
- Policy is now defined and industry/FDA gaining experience
- “A” process is critical; “the” process chosen by sponsor
- Questions remain; answers to be developed

- Thanks for your attention
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