FDA Perspective on Hepatitis D In Vitro Diagnostic Devices

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Topics for Discussion

1. FDA Regulation of In Vitro Diagnostics (IVDs)
2. FDA premarket review of IVDs
3. Example clinical study designs for Hepatitis D (HDV) IVDs

Premarket Risk Based Regulation

- Risk (and subsequently classification and submission type) is inherently tied to Intended Use of a device
  - **Class I** = Lowest risk: Usually exempt from FDA premarket review
  - **Class II** = Generally, moderate risk: Requires 510(k) clearance or de novo classification request
  - **Class III** = Highest risk: Requires premarket approval (PMA)

- De Novo Classification: Can potential risks to a patient be mitigated by special controls such as labeling, analysis of benefit/risk etc.

- There are currently no FDA cleared or approved HDV IVDs

https://www.fda.gov/medical-devices/overview-device-regulation/classify-your-medical-device

FDA premarket review of IVDs

- Review of IVDs is driven by the **intended use** of the device
  - The types of validation studies that are needed depend on the claims that are made in the intended use
- Considerations:
  - Purpose of the test: Diagnose, predict risk, monitor, identify population for whom a drug is effective, etc.
  - Disease or condition the device intended to diagnose, monitor, predict risk of, etc.
  - Test method (RT-PCR, ELISA, etc.)
  - Specimen type Serum, plasma, venous whole blood, capillary whole blood, dried blood spot, urine, saliva, etc.
  - Patient population: Symptomatic or asymptomatic
  - Context of use: In a laboratory, at the point of care (e.g., emergency rooms, doctor's offices), at home, etc.

PREMARKET REVIEW: ANALYTICAL STUDIES*

- Limit of Detection (LoD)/cut-off
- Limit of Quantitation (LoQ)
- Linearity
- Cross-reactivity
- Interference
- Carryover/contamination
- Matrix equivalency
- High dose hook effect
- Precision
- Genotype inclusivity/standards

*As applicable for technology and claim(s)

PREMARKET REVIEW: CLINICAL STUDIES

- Well-controlled clinical evaluations:
  - Clinical plan and protocol
  - Defined objective(s) and methods
- A test device that is the final design to be marketed
- Reproducibility across at least 3 sites
- Other evidence: case histories, literature where appropriate

Example Clinical Study Design
HDV RNA Tests

- Population: HBsAg positive patients with suspected HDV, prospective enrollment

- Design: Longitudinal study for disease progression

- If you have questions, come to talk to us using our Pre-submission program.

  Guidance on the Q-submission program: *Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program Guidance for Industry and Food and Drug Administration Staff (2021)*

Example Clinical study Design: HDV Antibody Tests

- Population: Subjects at risk for HDV, prospective-retrospective sample cohort

- Design: Compare results from candidate device to results derived from multiple well validated anti-HDV tests

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Example Comparator Algorithm for Clinical study: HDV Antibody Tests

Validated Test #1 (serology)	Validated Test #2 (serology)	Validated Test #3 (serology)	Algorithm Result
Positive	Positive	Positive	Positive
	Positive	Negative	
	Negative	Positive	
	Negative	Negative	Negative
Negative	N/A		Negative

Additional Resources

- Search for official FDA guidance documents and other regulatory guidance for all topics: *search for Qsub guidance and other submission guidances*
- Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program (fda.gov)
- https://www.fda.gov/medical-devices/premarket-submissions-selecting-and-preparing-correct-submission/de-novo-classification-request
- Premarket Approval (PMA) (fda.gov)
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