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FDA Regulation of Fecal Immunochemical Testing (FIT)

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Outline

- Overview of Medical Device Regulation
- FDA Review of FIT Assays
- Challenges in Regulation of FIT Testing

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Overview of Medical Device Regulation

Intended Use

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Medical Device Regulation

- FDA reviews submissions based on Intended Use and Indications for Use.
- Associated risk determines device classification and submission type (e.g. Premarket notification- 510(k), Premarket Approval-PMA)
  - Class I (low)
  - Class II (moderate) – 510(k)
  - Class III (high) – PMA
- Classification determines the scope of studies necessary to demonstrate device performance.

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Intended Use

- The **intended use** (IU) describes the general purpose of the device or its function, and encompasses the indications for use.
- The term **indications for use**, as defined in 21 CFR 814.20(b)(3)(i), describes the disease or condition the device will diagnose, treat, prevent, cure or mitigate, including a description of the patient population for which the device is intended.

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Intended Use: Factors to Consider

- Does the data support the intended use?
- Does the data demonstrate the device to be effective for its recommended use?
- Do the benefits outweigh the risks - false positive or false negative result?
- What warnings or limitations apply?

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FDA Review of FIT Assays

510(k) Pathway

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Review of FIT Assays: Premarket Notification

- FIT assays are cleared through the premarket notification (510(k)) regulatory pathway.
- Classified as a Class II device and cleared based on a determination of substantial equivalence to a legally marketed predicate.
- 510(k) Submission
  - Analytical Studies
  - Method Comparison
  - Labeling

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Review of FIT Assays: Performance Characteristics

- Analytical validation
  - Assay Cut-off
  - Precision Performance
    - Repeatability (within-run)
    - Reproducibility (lot-to-lot, site-to-site, between-run, between-device/instrument)
  - Specificity/Interferences
  - Assay Stability (test kit reagents)
    - Variability in temperature and humidity

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FIT Assay Performance Characteristics (Continued)

- Method comparison with clinical samples
  - Intended use setting (hospital laboratories, physician's offices, and over the counter)
- Pre-analytical variables
  - Specimen collection and handling
  - Stability (temperature, shipping)
- Impact of device technology
  - manual versus automated

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Labeling

- Final labeling must comply with the requirements of 21 CFR 809.10.
- Clear and concise directions for the end-user.
- Clear instruction for result interpretation and appropriate health care professional (HCP) follow-up or treatment.
- User and HCP Education
  - For example, FOB sample collection and analysis during a digital rectal exam (DRE) is inappropriate for colorectal cancer (CRC) screening.

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Other Considerations

- Number of Stool Specimens Required to Achieve Optimal Performance
  - Devices marketed for multiple bowel movements (2 or 3) vs. single sample test kits. Provide performance data consistent with the instructions for use (IFU).

*The marketing of a single stool sample analysis as an "adequate and effective annual screening test for colorectal cancer" is only appropriate with supporting device performance data to substantiate the claim.

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Other Considerations (Continued)

- Defined amount of stool sample is consistently obtained for FIT testing.
- For a quantitative claim for FOBT/FIT – FDA encourages submission of study proposals & questions via the Pre-Submission program
  - Benefit by capturing the Review Division's current recommendations
  - Please provide specific questions to obtain directed feedback (e.g. analytical and clinical study designs)

Pre-submission Guidance:
http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/UCM311176.pdf

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Challenges in Regulation of FIT Testing

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Review Challenges of FIT Tests: Premarket Considerations

- Do the analytical and clinical study designs support the intended use claims?
- Sample selection for analytical studies
  - Hemoglobin negative stool samples, instead of water or buffer, spiked with blood
- Appropriate data analysis (Agreement, Sensitivity and Specificity)

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Review Challenges of FIT Tests: Postmarket Surveillance

- Post market claims
  - Labeling
    - Must not be false or misleading
    - FIT tests: FDA ***cleared*** (Class II) vs. FDA ***approved*** (Class III)
  - Performance claims
    - Exaggerated (e.g. marketed sensitivity and specificity different than original clearance)

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Talk to FDA!

Thank you

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