An Introduction to pre-IDEs

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Agenda

- Introduction
- Pre-IDE Process
  - Sponsor proposal
  - Review by FDA review team
  - Meeting/Telecon with FDA
- Summary
- Question and answer period

What is a Pre-IDE?

- Free protocol review by FDA
- Allows informal discussion of complicated questions
  - Protocol review
  - Regulatory pathway
- Non-binding – not an agreement meeting
- Interactive and flexible

What a Pre-IDE is not:

- Not a prerequisite to an IDE
- Not a preliminary data review
- Not intended for studies already performed

Why would I need a pre-IDE?

- Familiarize FDA with a new technology
- Especially useful for
  - New intended uses
  - Novel devices
  - Companion diagnostics
- May prevent costly delays or errors

Goals

- Well prepared submissions
- Mutual education
- Shortened review times
- Focused validation studies
- Familiarize FDA with new technology
- Define possible regulatory pathways

When to submit a pre-IDE

- Intended use defined
- Patient population defined
- Ready to discuss protocols and regulatory pathway

Types of submissions where pre-IDE recommended:

- Waiver studies
- PMA or deNovo 510(k) anticipated
- New technologies
- Multiplex panels (e.g. genotyping; pathogens)
- Multivariate assays with composite score (IVDMIAs)
- Drug-device companion diagnostics
- Submissions where an IDE may be required

Is this your first submission? A pre-IDE may be useful.

Pre-IDE Process

- FDA review timeline: 60 days
- No user fee
- Interactive and flexible process

How do I get the process started?

- Submit written request and materials to the Document Mail Center*
- Format of interaction can be:
  - Written comments
  - Meetings:
    - teleconference, in-person

*** Where =** U.S. Food and Drug Administration
Center for Devices and Radiological Heath
Document Mail Center – WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

Pre-IDE Contents

- Device description / Test principle
- A clearly stated intended use
- *Analytical study design*
- *Clinical study design*
- *Statistical analysis plan*
- Specific questions for FDA

Intended Use

Should address the following:

- Analyte measured
- Purpose for measurement (Clinical Indication)
- Qualitative or Quantitative
- Intended Population
  - Adult /Children/Age limitations
  - Asymptomatic — Screening
  - Symptomatic — Diagnosis, prediction
  - Already diagnosed — Monitoring, prognosis
- Testing matrix (serum, saliva, etc.)
- Adjunctive or stand alone test

Intended Use will determine the nature of FDA feedback!

Analytical Validation

Objective of Analytical Validation

- Establish the analytical performance characteristics of the test (e.g., accuracy, reproducibility, etc.)

Describe:

- Studies to be performed
- Detailed proposed study design
- Samples (nature, number) to be tested

Recommended Readings

- CLSI guidelines:
  - EP05-A2 - Establishing precision
  - EP06-A - Establishing linearity
  - EP07-A2 - Interference studies
  - EP09-A2-IR - Method comparison studies
  - EP12-A2 - Qualitative tests
  - EP17-A - Limits of detection & limits of quantitation
  - EP21-A - Total error
  - C28-A3 - Reference ranges
- Statistical Guidance for Reporting diagnostic tests (http://www.fda.gov/downloads/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm071287.pdf)
- Predicate decision summaries

Clinical Validation

Objectives of the clinical Study

- To support the proposed intended use
- To establish the assay performance characteristics in “real world” conditions

New clinical study may not be necessary when existing data available (literature, etc.) that establishes clinical performance.

[Note: Regulatory review of literature for SE/S&E determination will be done during the 510(k)/PMA]

Clinical Validation

Objectives of the clinical Study

To establish clinical performance of device compared to an established endpoint or surrogate

- Clear, well-controlled study design
- Clearly show how endpoints are defined
- Clearly state how performance will be calculated
- Patients/samples should be selected using inclusion and exclusion criteria

Clinical Validation

- The number of patients/samples to be enrolled/used should be determined on sound statistical parameters
- Provide protocols for patient/sample information collection and documentation
  - How and by whom
- Consider having $\geq$ 3 clinical sites
  - International sites sometimes possible – clinical practice and test population considered
  - Provide contact information for all the PIs

Clinical Validation

Laboratory testing Procedures

- Clinical labs performing the testing during clinical trial should follow the procedure in the proposed product insert
- Specimen type should be defined
- Specimen collection, transport, process, and storage should be defined
- Quality control (incl. frequency and trouble shooting) for the assay should be defined

Statistical Plan

Study results—define *a priori*:

- How results are reported to sponsor
- How results are analyzed
  - Describe statistical tests
  - Describe how discrepant results are handled
- Definition of true positive, true negative, equivocal, and inconclusive results
- Primary endpoints
- Success criteria
- Power calculations

Administrative Issues

Establish:

- Study's start and finish dates
- Obligations of the PI and sponsor
- IRB & informed consent (non-US, Helsinki Accord) requirements
- Study site monitoring process
- SOPs for protocol deviation & change

Administrative Issues

Sponsors should ask ***specific*** questions to be addressed:

Good question =

"Given our power calculations, does FDA agree that our proposed sample size is reasonable?"

Bad Question =

"Does FDA agree with our proposed studies?"

Administrative Issues

Prior to submitting, you should get an independent:

- Clinical review
- Statistical review
- Clinical study design review
- Review for clarity

Protocol Review by FDA

- Review Team
  - Division review staff
  - Statistical reviewer
  - Medical Officer
  - External Consultants, e.g.,CDER, CBER, CDRH, CVM, CFSAN, CDC, NIH...
- Internal FDA discussions
- May request additional information
- FDA focus on specific sponsor questions

FDA Feedback

- Most current thinking and advice on your proposal
- Contains non-binding recommendations
- Closes Pre-IDE officially
- Can take many forms…

Pre-IDE Meeting with the FDA

All pre-IDE material should be sent in with meeting/teleconference request:

- Statement of the purpose of the meeting
- List of specific questions for FDA
- Preliminary proposed meeting agenda
- List of participating individuals
- Information packet
- Requested dates and times for the meeting

Administrative Issues

- Provide enough time before requested date of meeting for FDA to assemble review team and review pre-IDE material
- White Oak Visitor Procedures
  - Documentation of Foreign Visitors required at least 10 days before meeting
- Sponsors may take minutes of the meeting and submit them to the FDA

Summary

A Pre-IDE is:

- Free premarket proposal feedback
- Flexible
- Not binding on the FDA or the sponsor
- What you make of it!

Questions?

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