FDA Pre-IDE Submission

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AsTeC

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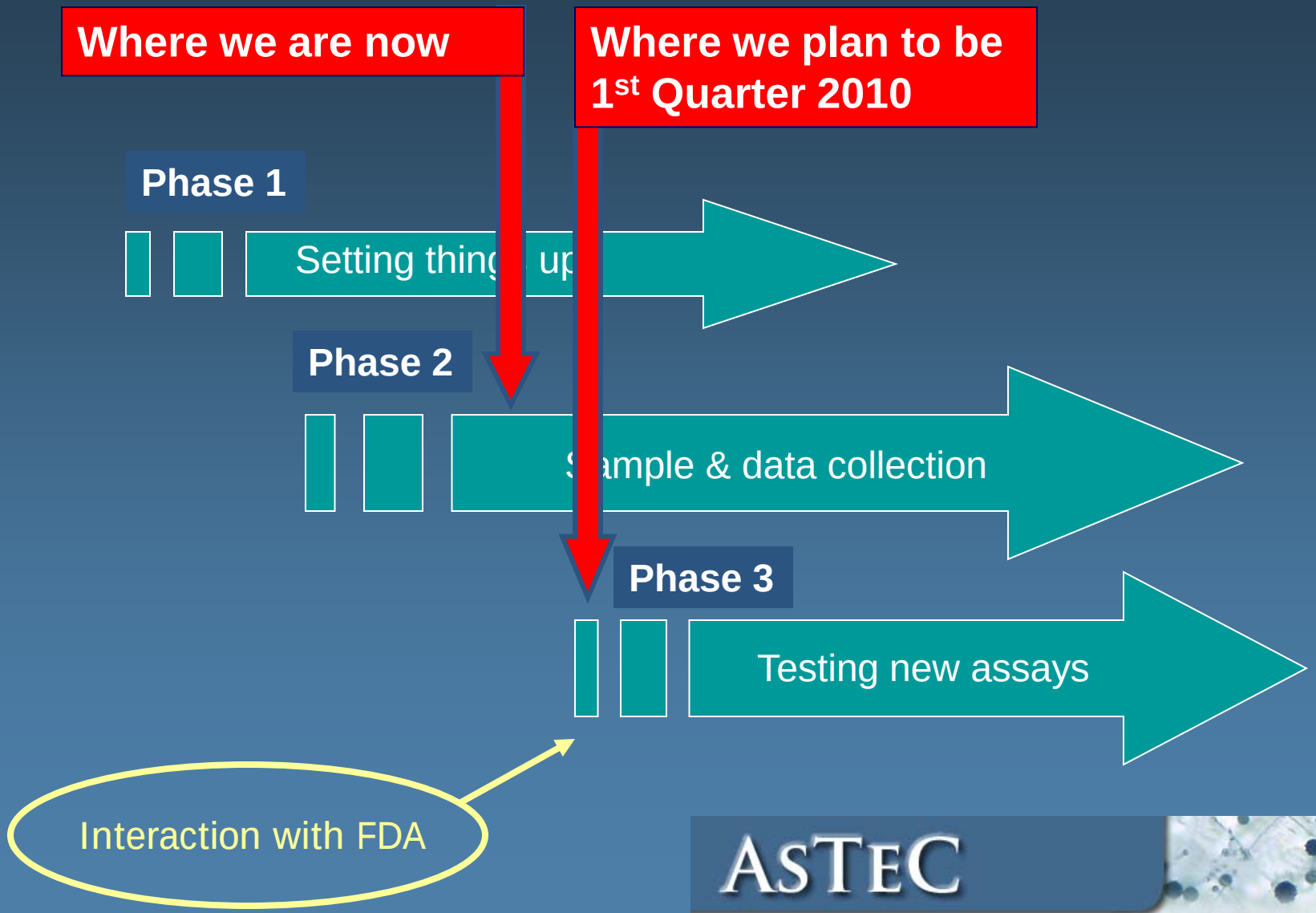
Project Timeline



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Bringing a Medical Device to Market

Regulatory Pathways

Premarket Notification (PMN) or 510(k)

- Demonstrate new device is at least as SAFE and EFFECTIVE (substantial equivalence) as a similar device in commercial distribution in the U.S.
- Device to which equivalence is drawn = "predicate device“

Premarket Approval (PMA) - more stringent than 510(k)

- Typically required for devices that pose “significant risk of illness or injury” or devices found not substantially equivalent to a predicate via 510(k)
- Includes submission of clinical data to support claims made for the device.
  - Sufficient scientific evidence to ensure device is safe/effective for intended use

Investigational Device Exemption (IDE)

- Allows investigational “significant risk” device to be used in a clinical study to collect data required to support a PMA or 510(k) application

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Classification of Medical Devices

- Device classification determines regulatory requirements
- Classification based on intended use & risk to patient
- Medical devices are assigned into Class I, II, and III
- Regulatory control increases from Class I to Class III
  - Most Class I devices - exempt from **Premarket Notification 510(k)**
    - Subject to Marketing Requirements
      - Registration/Listing, Labeling, GMP
  - Most Class II devices - **Premarket Notification 510(k)**
  - Most Class III devices - **Premarket Approval (PMA)**
    - Support or sustain human life, are of substantial importance in preventing impairment of human health, or present potential, unreasonable risk of illness or injury

FDA Pre-IDE Process

- Informal interaction with key FDA staff who will evaluate the application
- Facilitate clearer understanding of FDA's expectations regarding
  - appropriate regulatory pathway
  - proper approach to refine/define clinical data
  - statistical analyses
  - answers to critical questions related to medical device clinical trial design before submission of a formal IDE.
- Means for gaining feedback for non-significant risk, exempt, or post-market studies which do not require an IDE, but which will generate data to support an eventual marketing submission

AsTeC - FDA Pre-IDE Meeting

Purpose:

1) Familiarize FDA with AsTeC resources and capabilities
2) Obtain FDA feedback regarding the scientific merits of the protocols developed per the AsTeC objectives and statement of work

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AsTeC - FDA Pre-IDE Meeting

12/08/08 DMID retained consultant to facilitate FDA discussions between:

FDA and AsTeC + Sponsors

08/18/09 Pre-IDE Meeting requested by letter

Included collection, processing, & test evaluation protocols

10/27/09 Received FDA Review Summary of materials submitted

11/06/09 Final meeting agenda / questions for Pre-IDE submitted to FDA

11/17/09 Face-to-face Pre-IDE meeting between AsTeC, DMID, and FDA

U.S. Food and Drug Administration

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Center for Devices and Radiology Health

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Office of In vitro Diagnostic Device Evaluation & Safety

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Division of Microbiology Devices

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Sampling of Questions Submitted from AsTeC to the FDA

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Regarding qualification of AsTeC specimens/data...

Are specific changes or additions to the protocol in the following areas that the agency believes are necessary in order for AsTeC specimens/data to qualify for use in a device application?

a.) specimen collection,

b.) specimen processing and/or banking,

c.) clinical data collection, or

d.) specimen testing.

Regarding use of archived vs. fresh samples...

Will the FDA require a certain percentage of data from fresh, non-archived specimens, in addition to data generated from AsTeC specimens, in support of a Premarket Notification or Premarket Approval application for a device?

Regarding use of MSG/EORTC definitions as gold standard...

Is the use of the EORTC/MSG definition for invasive aspergillosis satisfactory for use as the “reference method for diagnostic certainty”?

a.) Are modifications to the definition of <u>proven</u> invasive aspergillosis allowable? For example, use of immunohistochemistry for delineating septate hyphae in tissue as A*spergillus* versus other non-*Aspergillus* mould in cases for which fungal culture of tissue was negative.

b.) Will the agency accept cases of probable invasive aspergillosis for which the only microbiologic criterion for determining “probable” disease status was a positive galactomannan test?

Regarding selection of a predicate device...

For new diagnostic devices for invasive aspergillosis that measure an analyte other than galactomannan, will the galactomannan assay be used as the predicate device?

Regarding different *Aspergillus* species...

Will the agency require a percentage of specimens from patients infected with different *Aspergillus* species (i.e. *A. fumigatus, A. flavus, A. niger, A. terreus, etc.*)?

Regarding development of the Calibrator...

AsTeC is working with other NIH contractors to develop a calibrator of high quality genomic *Aspergillus* DNA as a tool for verifying and comparing performance of molecular tests for diagnosing invasive aspergillosis. At what stage of development should we involve the agency in critiquing or planning the development of the calibrator?

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Getting new diagnostic tests for Invasive Aspergillosis into clinical care sooner.

www.astecdiagnostics.org

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