Introduction to the United States Food and Drug Administration (FDA) and FDA Inspection Process

VOICE

2011 MTN Annual Meeting

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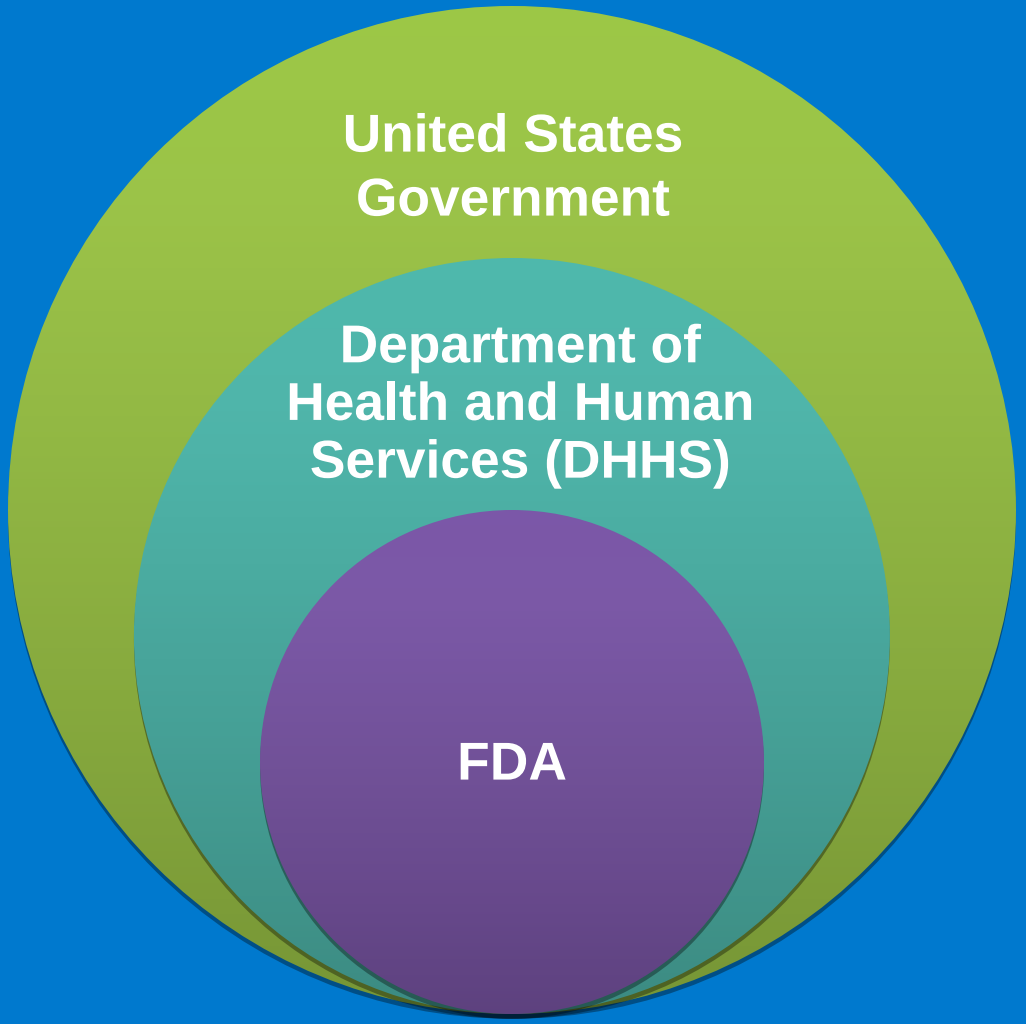
Objectives

- Understand why and how VOICE may be inspected by FDA
- Review proposed timeline for inspection preparation
- Get your feedback

FDA

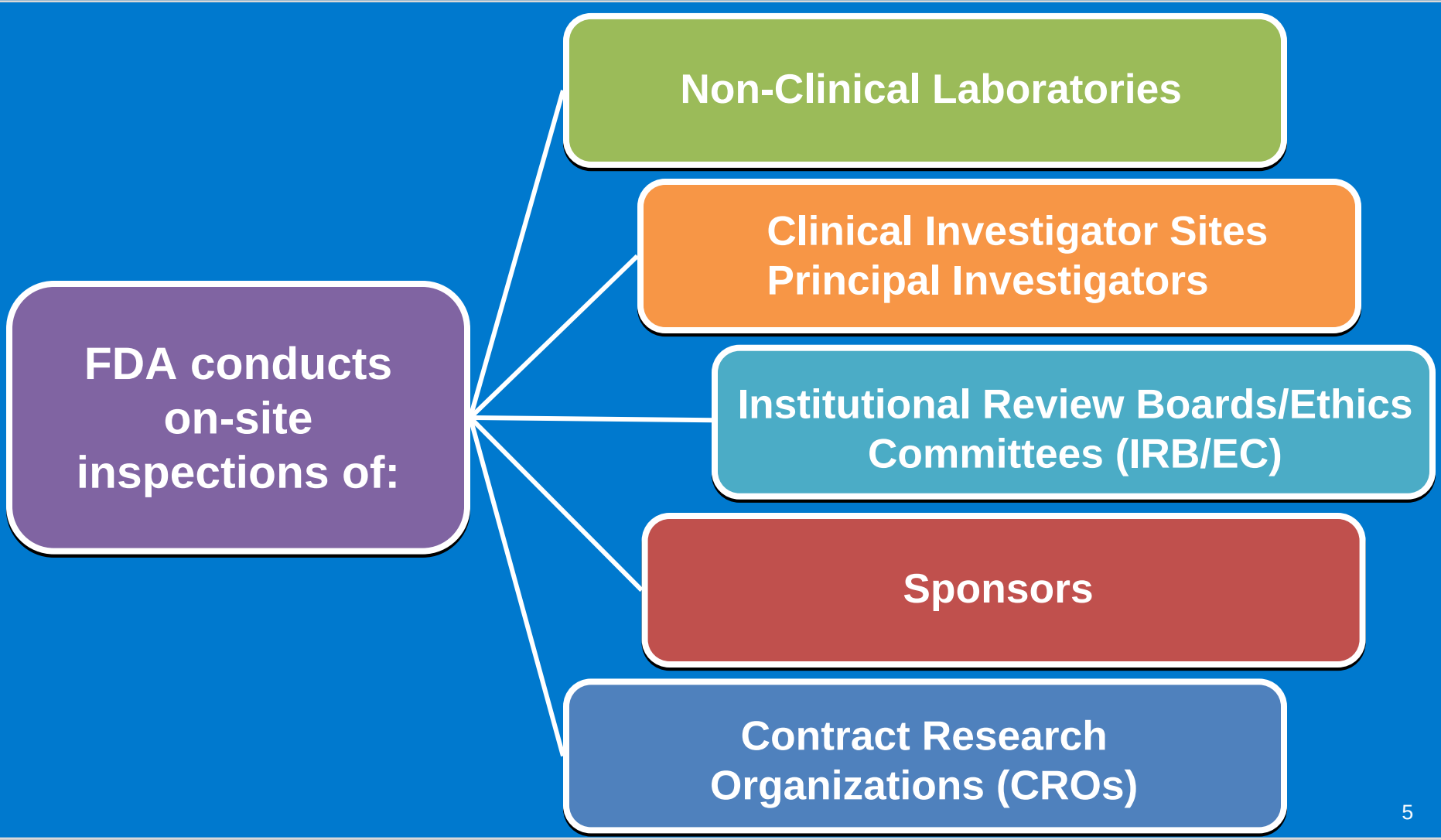
The FDA is an agency within the Department of Health and Human Services (DHHS) of the United States Government.



Background

- US Food, Drug, and Cosmetic Act requires all new investigational drugs undergo clinical trials
- Role of US FDA
  - Review clinical trial protocol
  - Review sponsor marketing application
  - **Inspections of clinical trials sites, including participant charts, pharmacies, etc.**
- Ensures safety of participants, consumers
  - Verification that data are accurate and reliable
  - Verify compliance with regulations and GCP guidance
  - Verify control of study product

FDA Inspection



Why inspect VOICE?

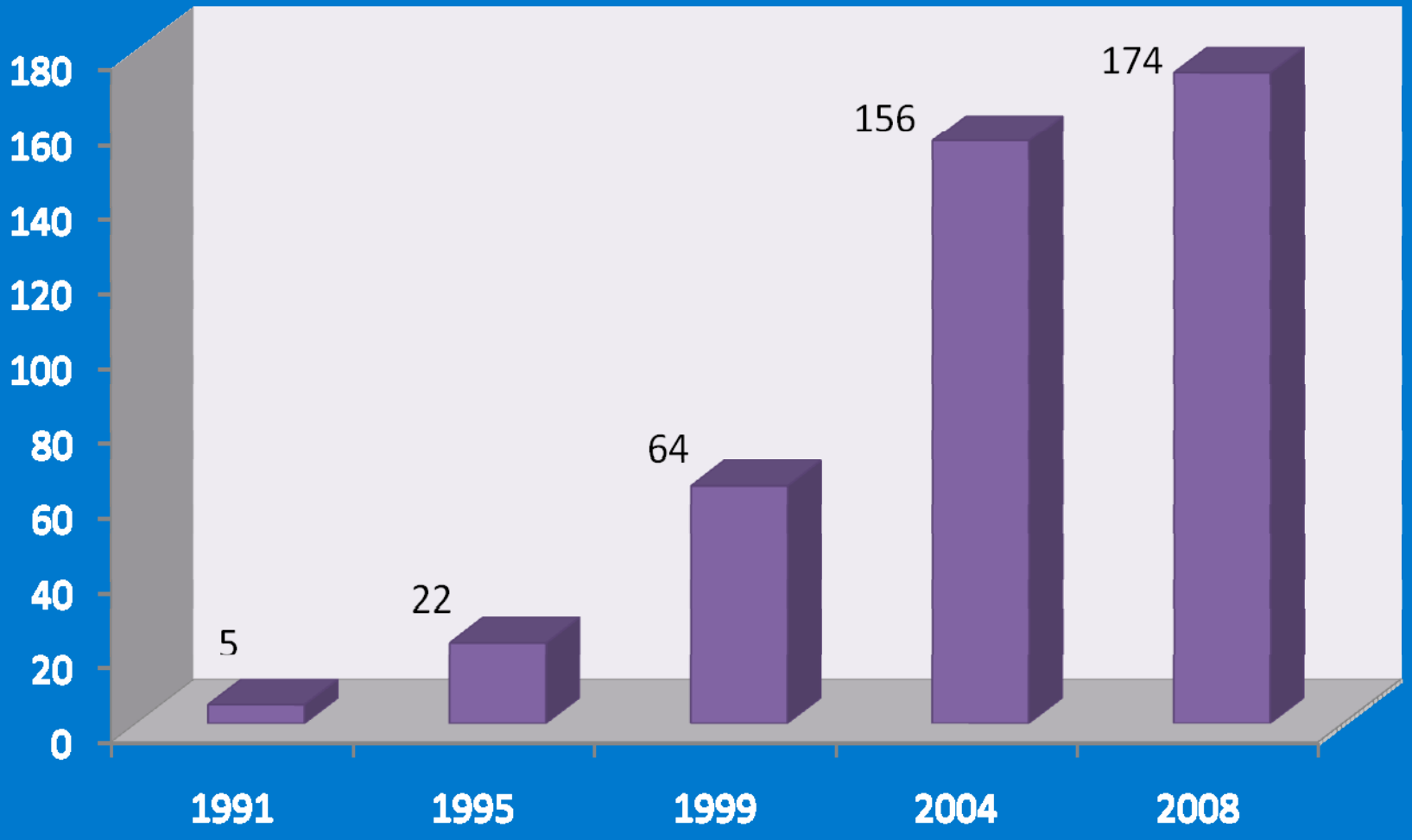
- FDA agreed to use VOICE as second pivotal trial for the TFV gel licensure application
- Data will support marketing applications
  - Oral drug – supplementary marketing
  - Gel – initial application
- Large volume of participants – 5,000
- High enrollments at some sites
- "International inspections are generally assigned when the studies covered are part of a marketing application to FDA and provide data critical to decision-making on product approval."
  – FDA Compliance Program Guidance Manual

International Inspections

- 40-65% studies investigating FDA-regulated products are conducted outside US
- In 2008, 80% of marketing applications received by the FDA contained data from international clinical studies
  - 78% of participants involved in studies supporting these applications enrolled at international sites
  - 54% of the clinical sites conducting these studies were located outside the United States

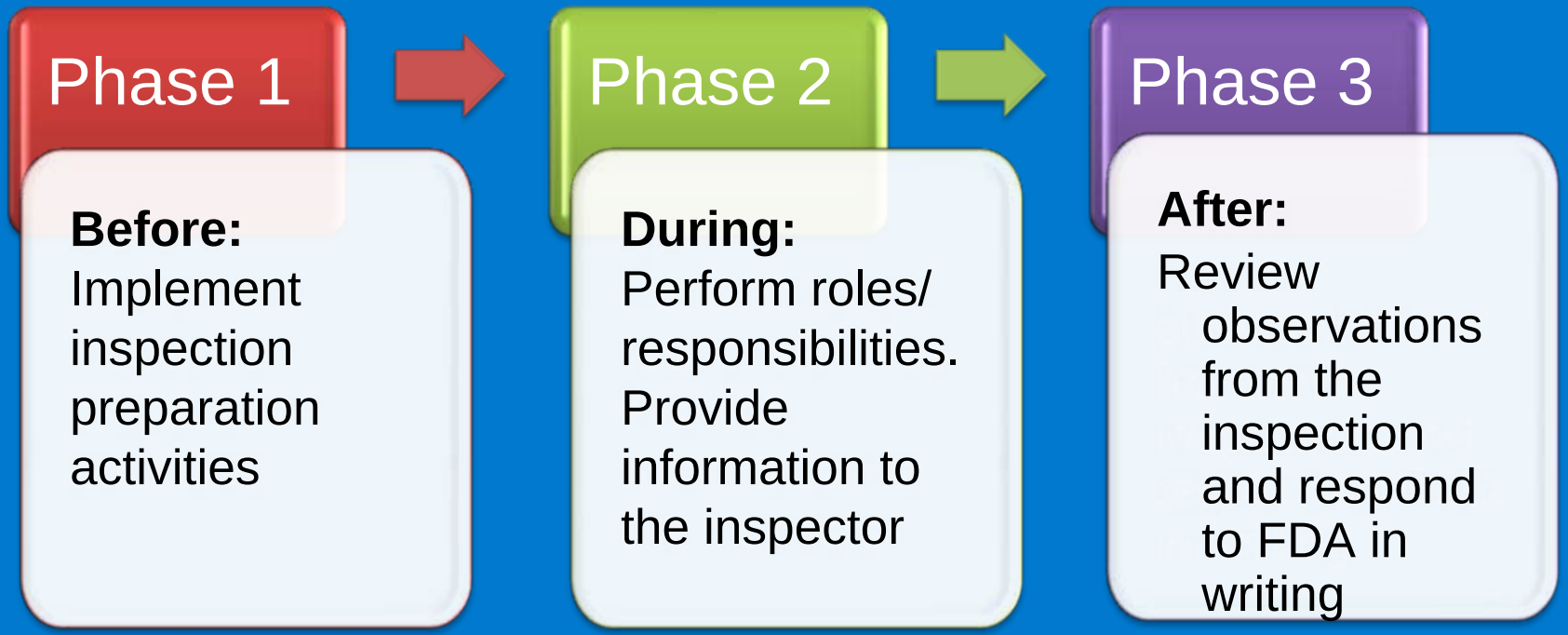
Challenges to FDA's Ability to Monitor and Inspect Foreign Clinical Trials, DHHS, June 2010

FDA Inspections of International Sites 1991 - 2008



Overview of the FDA Inspection Process

Three Distinct Phases of an FDA Inspection:



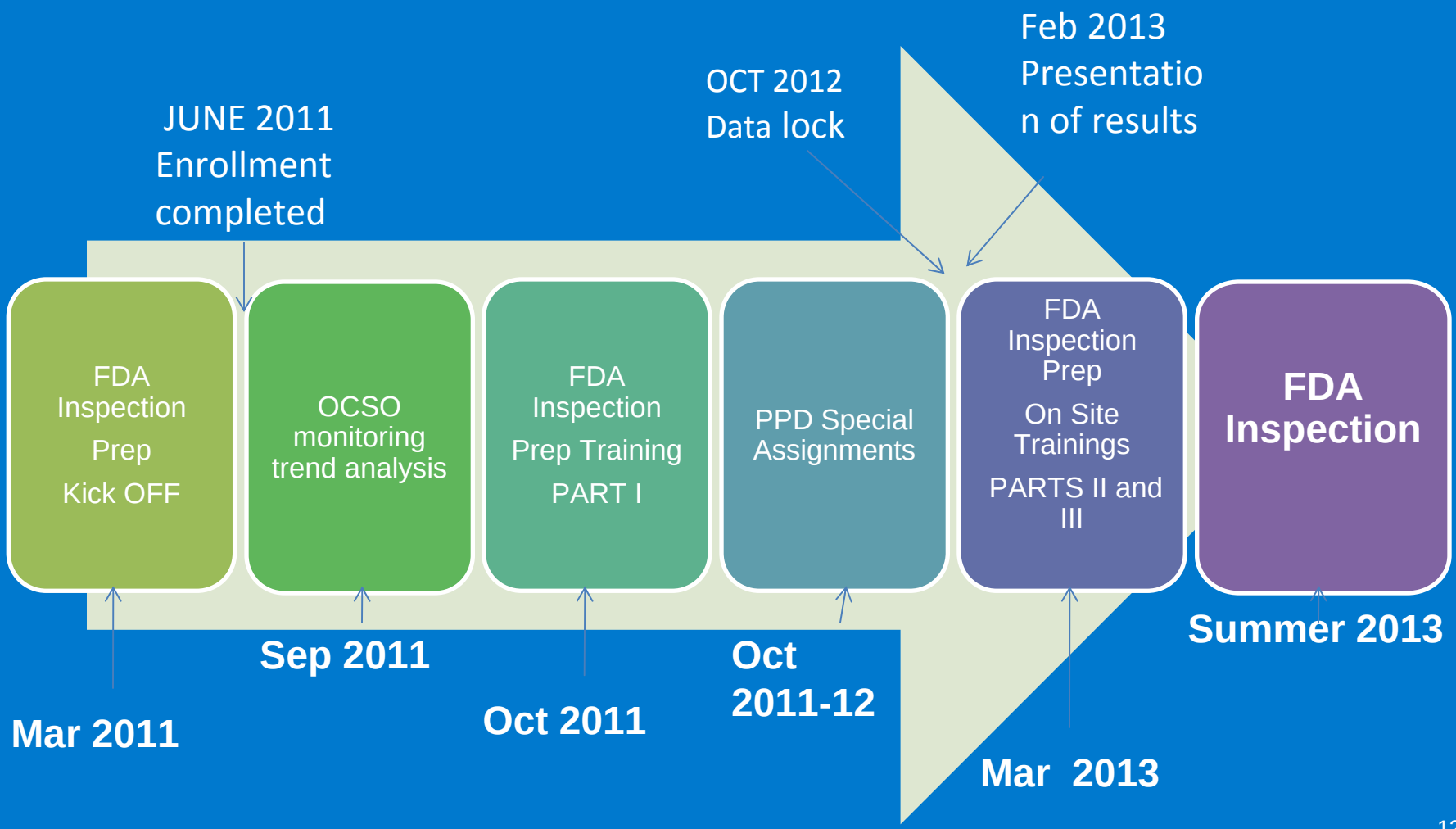
Which sites will be inspected?

- We don’t yet know for certain
- Strong contenders
  - High volume sites
  - Sites with high number of HIV endpoints
  - Sites identified as having potential issues with data quality or protocol compliance
  - But, could be any number of VOICE sites!
- **All sites should be prepared**

Dealing with the unknowns

- Exact timing of inspections?
  - Can estimate based on other trials
- Who will be inspected?
  - Again, can formulate reasonable possibilities
- What will be inspected?
  - Guidance will be given to sites on key areas of focus for preparation
  - **Example: documentation related to primary endpoint confirmation**

FDA Inspection Preparation Timeline



What sites can do now to prepare?

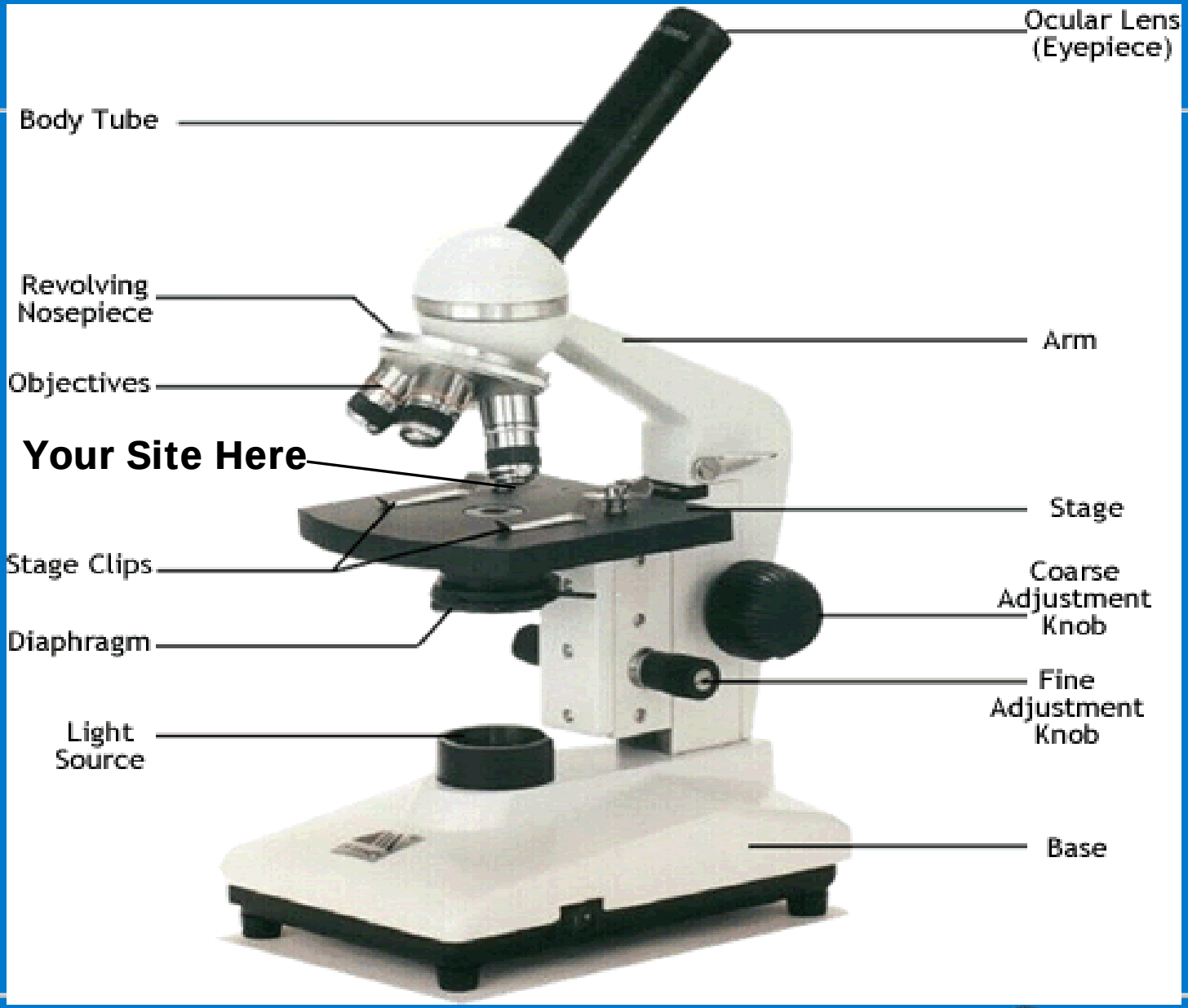
- Develop a FDA Inspection "SWAT TEAM" (clinical, regulatory, pharmacy, and lab)
- Implement FDA prep checklist
  - Use OCSO monitoring trend report and protocol deviation summary as tools for internal QA/QC
- Ensure timely submission of CRFs and response to queries to SDMC
- Ensure all monitoring report findings resolved
- Ensure Regulatory Binder is complete and orderly
- Re-evaluate and update CQMP

IPrEx

December 09	• Enrollment completed
August 10	• PPD CRS Contract Monitoring Trend Analysis completed • Data SNAPSHOT for primary analysis
December 10	• Results Announced • PPD CRS Contract Trainings started
April 11	• Gilead submits supplemental NDA application to FDA • **FDA has 60 days to inspect sites**

Summary

- If VOICE results show efficacy, there is high likelihood that sites will be inspected
- Who will be inspected and when remains to be determined
- Advance preparation is KEY to a successful FDA inspection and LESS STRESS!


Ocular Lens
(Eyepiece)
Body Tube
Revolving
Nosepiece
Arm
Objectives
Your Site Here
Stage
Stage Clips
Coarse
Adjustment
Knob
Diaphragm
Fine
Adjustment
Knob
Light
Source
Base