Special Concerns in *in vitro* Diagnostic Trials

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Learning Objectives

- What is unique about *in vitro* diagnostic clinical trials?
- What are the particular challenges faced by sponsors and sites when it comes to *in vitro* diagnostic clinical trials?
- What are some practical solutions to these challenges?

WHY ARE IN VITRO DIAGNOSTICS (IVD) REGULATED AS DEVICES?

- "A medical device is…an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent…which does not achieve its primary intended purposes through chemical action within or on the body…and which is not dependent upon being metabolized for the achievement of its primary intended purposes."
  - 21 USC 321 (h)
  - FDC Act 201(h)

Definition of an in vitro Diagnostic

- "Reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae…for use in the collection, preparation, and examination of specimens from the human body."

—21CFR 809.3

So how do IVDs differ from other medical devices?

- Simply put…IVDs include products used to collect and/or examine specimens after they are removed from the body.

Definition of a "Human Subject"

- Includes
  - "Subject is an individual on whom or on whose specimen an investigational device is used."
- All human subject regulations apply in IVD studies

Informed Consent in IVD Trials

- The informed consent process has special nuances in IVD clinical trials
  - —Prospective sample collection for future studies
  - —Leftover samples

Intended Use of the IVD

- "Intended Use" is driving force of the scientific review
  - Who will be tested?
  - What are the appropriate specimens?
  - How results may be used?

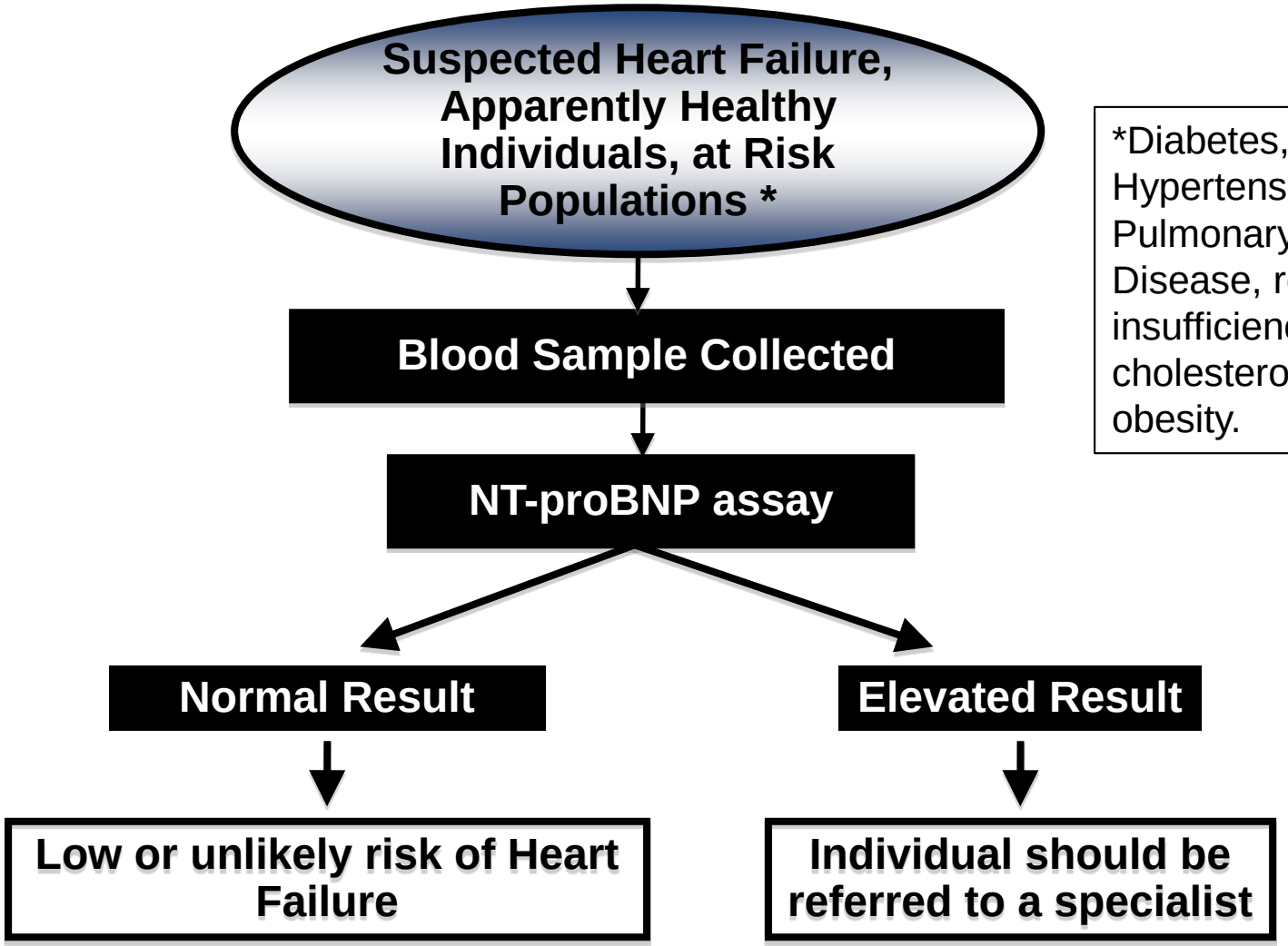
Challenges & Solutions

- The biggest challenge is understanding first principles
  - Analytical Performance Characteristics
    - Reliability and accuracy of analyte measurements
  - Clinical Performance Characteristics
    - Clinical sensitivity and specificity
    - Positive and negative predictive values
  - Labeling
    - Intended use, design, directions for use, etc.

Cardiac Biomarker NT-proBNP

- NT-proBNP = N-terminal fragment Brain natriuretic peptide BNP
- FDA Cleared claims for NT-proBNP
  - Aid in the diagnosis for patients with suspected heart failure
  - Risk stratification for patients with
    - Congestive Heart failure
    - Acute coronary syndromes
  - Aid in the assessment of increased risk of CV events and mortality in patients at risk for heart failure with
    - Coronary artery disease

Patient Testing



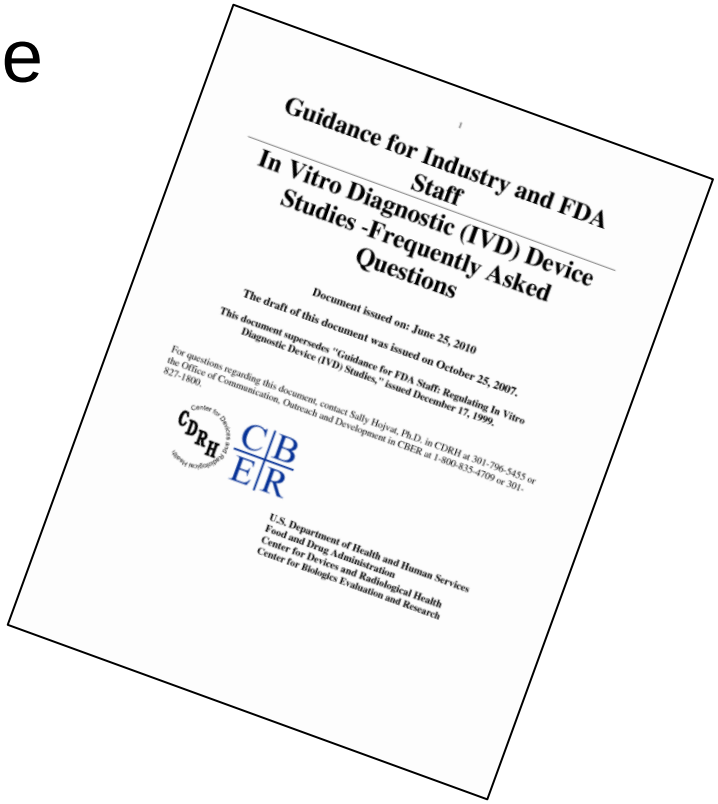
*Diabetes, Hypertension, Pulmonary Artery Disease, renal insufficiency, high cholesterol and obesity.

SUMMARY

- IVDs are medical devices
  - All regulations apply accordingly
- Informed consent issues bear special attention
- The primary solutions to challenges in IVD clinical trials involve a thorough understanding of
  - Analytical Performance Characteristics
  - Clinical Performance Characteristics
  - Labeling

Resource Material

- FDA Guidance Document: In Vitro Diagnostic (IVD) Device Studies—Frequently Asked Questions
  - —June 25, 2010



Guidance for Industry and FDA Staff

In Vitro Diagnostic (IVD) Device Studies -Frequently Asked Questions

Document issued on: June 25, 2010

The draft of this document was issued on October 25, 2007.

This document supersedes "Guidance for FDA Staff: Regulating In Vitro Diagnostic Device (IVD) Studies," issued December 17, 1999.

For questions regarding this document, contact Sally Hojvat, Ph.D. in CDRH at 301-796-5455 or the Office of Communication, Outreach and Development in CBER at 1-800-835-4709 or 301-827-1800.

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