Diagnostic Considerations

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Rare Diseases

- Rare diseases vary with regard to severity and organ systems affected

- Diagnostics play an important role
  - Correct identification of disease is one step towards getting the help needed
  - Diagnostic devices – in vitro laboratory testing, genetic tests, radiographic imaging, EKGs, EEGs, stethoscopes, endoscopes are all devices that aid in arriving at a diagnosis

What is an IVD?

World of IVDs

- $10-15 Billion industry for raw materials

- $30-50 Billion for testing

- 10 Billion lab tests in > 200,000 labs

- Involved in more than 70% of medical decisions

Medical Device Amendments of 1976

- Premarket review
- Different submission packages
  - 510(k)s and PMAs
- Same scientific questions

Analytical Performance

- Accuracy
- Precision
- Analytical specificity
- Analytical sensitivity

Clinical Performance

- Clinical sensitivity

- Clinical specificity

- Predictive values

Issues with Pediatric Devices for Rare diseases

- Analytical Validity
  - Specimen
- Clinical Validity
  - Clinical Studies
  - Risk Benefit

Specimen

- Availability
  - Difficult to get
  - Difficult to get enough
- FDA solutions
  - Use of cell lines
  - Use of plasmids.
  - Fewer samples.
  - Sample pooling when appropriate

Clinical Studies Challenges

- Adequate representation across FDA defined pediatric groups

- Limited number of patients and ethical issues

- Extremely rare diseases

- Clinical truth

Clinical Studies FDA Solutions

- Use of well-recognized pediatric reference intervals

- Use of literature support

- Use of retrospective sample testing with enrichment with positive samples

- Use of statistical analysis plans that account for missing data

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Questions?