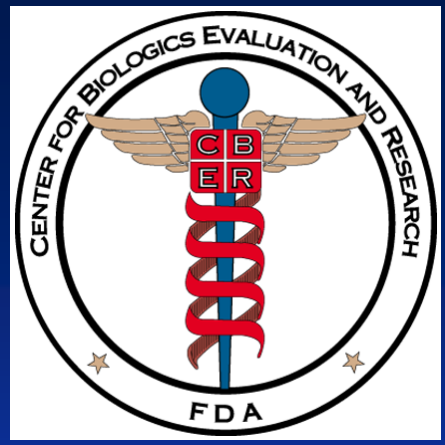

Regulation of In Vitro HIV Drug Resistance Genotype Assays

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FDA/CBER/OBRR/DETTD

New Final Rule: 8/8/2007

- 21 CFR 866.3950 – Assay, Genotype, HIV Drug Resistance, In Vitro

  In vitro HIV drug resistance assays are devices that consist of nucleic acid reagent primers and probes together with software for predicting drug resistance/susceptibility based on results obtained with these primers and probes, for use in detecting HIV genomic mutations that confer resistance to specific antiretroviral drugs, as an aid in monitoring and treating HIV infection.

Class II Special Controls Guidance: 8/8/2007

- Purpose
  - To support reclassification of these assays from Class III to Class II
  - To ensure reliability of these assays for recognized mutations and to show how these assays may be developed for review by FDA as Class II medical devices
- General requirements
  - Conform to general controls of the FD&C Act, including premarket notification requirements
  - Address specific risks to health associated with these assays
  - Obtain substantial equivalence determination from FDA prior to marketing the device

Overview of Guidance

- Risks to health
  - Subjecting patients to unnecessarily high viral loads or to unnecessary risks of side effects due to administration of inappropriate drugs
- Recommended mitigation measures
  - Data to support performance characteristics
  - Other considerations

Performance Characteristics

- Critical components of assays
  - Assay that determines and reports the genotype
  - Interpretation algorithm
- Data should be submitted to support performance characteristics of device, either:
  - Extensive analytical studies for listed mutations
  - Less extensive analytical data combined with clinical data showing performance of test as aid in treatment of subjects with HIV (indications for use may be limited)

Studies to be Performed

- Performance of the interpretive algorithm
  - Validation of phenotypes predicted by genotyping: in vitro studies
  - Verification of phenotypes predicted by genotyping: in vivo studies

Studies to be Performed, cont.

- Performance of the assay in determining genotype
  - Analytical sensitivity, range of detectability, precision, reproducibility, lot acceptance testing, specificity, assay interference, reagent characterization, specimen collection and handling conditions
- Stability
- Assay performance on clinical specimens
  - Sensitivity, specificity, reproducibility
- Clinical trial data showing performance as an aid in treatment of subjects with HIV
  - Not necessary if complete analytical studies performed

Additional Considerations

- Design controls
- Statistical methods
- Devices used to generate data for submission
- Instruments and software
- Product modification
- Labeling
- Special 510(k) to update interpretation algorithms
  - New information on resistance mutations

Additional Information

- Federal Register: Medical Devices: Immunology and Microbiology Devices: Classification of In Vitro Human Immunodeficiency Virus Drug Resistance Genotype Assay: Final Rule – 8/8/07

  http://www.fda.gov/cber/rules/fr-pmhivdrg.htm

- Class II Special Controls Guidance Document: In Vitro HIV Drug Resistance Genotype Assay

  http://www.fda.gov/cber/gdlns/pmhivdrg.htm