Overview of Device Regulation

Secretary's Advisory Committee On Heritable Disorders In Newborns And Children

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FDA Regulation of IVDs

- General introduction to Medical Devices and IVDs
- Review considerations
- Challenges for neonatal screening devices
- Resources

FDA Regulation of IVDs

- Federal Food, Drug, and Cosmetic Act of 1938 (The Act)
- Medical Device Amendments of May 28, 1976 – classified all existing IVDs
- Clinical Laboratory Improvement Act (CLIA) 1988
- FDA Modernization Acts of 1997 and 2007

Medical Device Amendments of 1976

Regulation of all Medical Devices includes:

- General controls (e.g., current Good Manufacturing Practices)
- Registration and listing
- Good manufacturing practices
- Reporting of adverse events
- Risk based regulation by intended use

What is an IVD?

"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 in man. … for use in the collection, preparation, and examination of specimens from the human body." [21 CFR 809.3]

Used in clinical laboratories & other settings
(e.g., Point-of-Care/Over-the-Counter)

What is an IVD?

In Vitro Diagnostic Tests for :

- Diagnosis
- Screening
- Epidemiology/Surveillance
- First Response

- **Not** Environmental Screening

Intended Use

As for other devices, IVD review is driven by the intended use of the device

The type of review [510(k), PMA, etc.] and the types of validation studies that are needed depend on the claims that are made in the intended use

Device Regulation

FDA Regulates IVDs by the intended use and the risk of an incorrect result:

Class I – Low risk – Usually exempt from Premarket FDA review

Class II – Moderate risk – requires a predicate device - requires 510(k) clearance

Class III – High risk and novel intended uses - requires premarket approval (PMA)

Intended Use

The risk of an IVD is based on the consequences of a false result

Examples:

High risk – HIV, tuberculosis

Lower risk – Calcium, pregnancy

Intended Use

"Moderate Risk" intended uses usually require premarket review in the form of a premarket notification [510(k)] submission

- The company submits information describing how the device is "substantially equivalent" to legally marketed devices
- Submissions may include clinical data

"High Risk" intended uses require premarket review in the form of an application for Pre-Market Approval (PMA)

- This sometimes includes devices with new intended uses, technologies/methodologies, scientific questions
- The company submits information describing the safety and effectiveness of the device, usually including the device performance in clinical trials

Premarket Review

All IVDs must establish adequate:

Analytical performance

- How accurately does the test measure the analyte?
- How reliably?

Clinical performance

- How reliably does the test measure the clinical condition?

Labeling (21 CFR 809.10)

- Adequate instructions for use
- Intended use, directions for use, warnings, limitations, interpretation of results, performance summary

Key Elements of a Submission

- Intended use/indications for use
- Device description
- Analytical validation
- Clinical validation
- Instrument and software validation, if applicable
- Labeling (package insert)
- Manufacturing, design controls, quality system requirements (PMA only)

Intended Use

The Intended Use is the driving force of the review:

The ABC Non-derivatized MSMS kit is intended for the measurement and evaluation of amino acids, succinylacetone, free carnitine, and acylcarnitine concentrations from newborn heel prick blood samples dried on filter paper.

Quantitative analysis of these analytes (listed in the tables below) and their relationship with each other is intended to provide analyte concentration profiles that may aid in screening newborns for metabolic disorders.

Analytical Performance

Repeatability/Reproducibility

- Will I get the same result in repeated tests over time?
- Will I get the same result as someone else testing the same sample?

Accuracy

- Will I get results that are the same as “Truth”?
- “Truth” – may be a reference method, clinical endpoint, predicate device, etc…

Limit of Detection, Potential Interferences / Cross-Reactivity, Cross-contamination / Carry-over, etc

Clinical Performance

Clinical performance – clinical validity

- Device must have a clinical indication/clinical validity

May be based on:

- Existing clinical data
- New clinical trial data
- Review of information in the literature
- Current clinical knowledge

Clinical Performance

Samples/Populations

- Should represent Intended Use population
- Prospectively collected (ideal)
- If retrospective, should reflect intended use population, investigate sample storage
- Clearly defined inclusion/exclusion criteria
- # of positives statistically appropriate

Sites - Minimum of 3

Challenges

- Difficult to obtain patient samples, especially true positives
  - work with State Health Laboratories
- Must consider special circumstances
  - potential interferences from drugs and endogenous substances, cross-reactivity during device evaluation
  - sample collection issues

Neonatal Screening

FDA cleared devices:

- For inborn errors of amino acid, free carnitine and acylcarnitine metabolism
- TSH
- 17α-Hydroxyprogesterone for classical congenital adrenal hyperplasia
- Immunoreactive trypsin (IRT)
- Biotinidase deficiency

Other Pathways

- De Novo Petition for Classification
- Reclassification Petition (e.g. tacrolimus)
- Investigational Devices
- Humanitarian Device Exemption (HDE)
- Emergency Use Authorization (EUA)
- Compassionate Use (IDE)

FDA Guidance Documents

- Points to Consider for Portable Blood Glucose Monitoring Devices Intended for Bedside Use in the Neonate Nursery
- Guidance on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable
- In Vitro Diagnostic (IVD) Device Studies – Frequently Asked Questions
- Statistical Guidance on Reporting Results from Studies Evaluating Diagnostic Tests
- Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices etc.. etc..

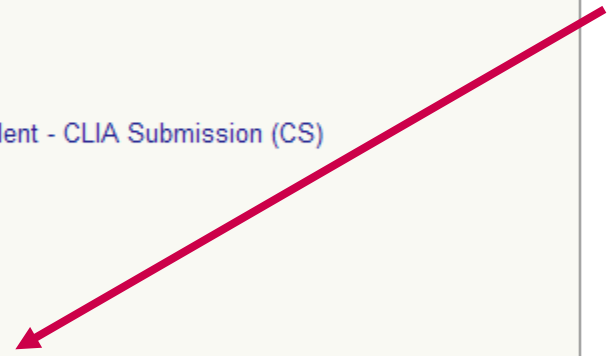
Transparency

510(k) Database: http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm

Transparency

New Search | Back To Search Results

Device Classification Name	System, Test, Amino Acids, Free Carnitines And Acylcarnitines Tandem Mass Spectrometry
510(K) Number	K083130
Device Name	NEOBASE NON-DERIVATIZED MSMS KIT, MODEL 3040
Applicant	PERKINELMER, INC. 8275 Carloway Road Indianapolis, IN 46236
Contact	Kay A Taylor
Regulation Number	862.1055
Classification Product Code	NQL
Date Received	11/13/2008
Decision Date	07/09/2009
Decision	Substantially Equivalent - CLIA Submission (CS)
Classification Advisory Committee	Clinical Chemistry
Review Advisory Committee	Clinical Chemistry
Summary	Summary
FDA Review	Decision Summary
Type	Traditional
Reviewed By Third Party	No
Expedited Review	No



Transparency

510(k) SUBSTANTIAL EQUIVALENCE DETERMINATION
DECISION SUMMARY
ASSAY ONLY TEMPLATE

A. 510(k) Number:
k083130

B. Purpose for Submission:
New device

C. Measurand:
Amino acids, free carnitine, acylcarnitines, and succinylacetone

D. Type of Test:
Quantitative measurement by mass spectrometry

E. Applicant:
PerkinElmer, Inc.

F. Proprietary and Established Names:
NeoBase Non-derivatized MSMS kit

G. Regulatory Information:
1. Regulation section:
   21 CFR §862.1055 Newborn screening test system for amino acids, free carnitine, and acylcarnitines using tandem mass spectrometry

Thank you!

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