U.S. FOOD & DRUG ADMINISTRATION

AvertD Panel Meeting: FDA De Novo Training

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Medical Device Classification (summary)

- **Class I devices: general controls**
  - Registration and listing of manufacturing facilities
  - Quality System requirements (including good manufacturing practices)
  - Medical Device Reporting (adverse events)
  - Prohibitions against misbranding/adulteration

Generally **exempt** from FDA premarket review

- **Class II devices: general controls and special controls**, which can include:
  - Specific bench testing requirements
  - Specific labeling requirements
  - Specific clinical or postmarket requirements

Devices are **cleared** through the **510(k)** process and "substantial equivalence"

- **Class III devices: general controls and premarket approval** (PMA)
  - Demonstrate "reasonable assurance of safety and effectiveness" for the device from first principles
  - Review of manufacturing changes to the device
  - Ongoing annual reporting requirements
  - Conditions of approval, including postmarket requirements

Devices are **approved** through **PMA** process

What Is a De Novo Request?

- A type of premarket submission, like a 510(k) or PMA (obtaining marketing authorization for a device)
- Intended for **new types of devices** that are low-to-moderate risk that are otherwise automatically classified into class III
- Request to classify the device into class I or class II based on **reasonable assurance of safety and effectiveness** (**not substantial equivalence**)
- If granted:
  - FDA **creates a new classification regulation**
  - the new device type is regulated through 510(k), if class II
  - the De Novo device serves as the first predicate device of its kind

Is the Product Eligible for De Novo?

- **Must be a medical device (Section 201(h) of FD&C Act)**
- **Must not fit into any existing classification regulation**
  - Doesn't fit into existing Class I/II regulation, i.e., no predicate device (not substantially equivalent (NSE))
    - Includes unclassified preamendments devices
  - Doesn't fit into existing Class III regulation
- **No approved PMA(s) for same device type**

Classification Process – Goals

1. Determine if probable benefits outweigh probable risks
2. Identify probable risks to health for the device/product
3. Determine level of control needed:
   - general controls only = class I
   - general controls + special controls = class II

Together, these provide reasonable assurance of safety and effectiveness.

Benefit-Risk Assessment

- Based on totality of evidence in the De Novo request
- Assessment of probable benefits
- Assessment of probable risks
- Assessment of additional factors, for example:
  - Uncertainty
  - Patient perspectives
  - Addressing unmet medical need

New Classification Regulation

- Number (e.g., 21 CFR 862.XXXX)
- Name (name of device type)
- Identification
  - Intended use(s)
  - Key technological characteristics
  - Describes what FDA believes to be a single device type with a shared intended use and technology

Risk/Mitigation (R/M) Table

Identified Risks to Health	Mitigation Measures
Infection	Reprocessing validation Labeling
Adverse tissue reaction	Biocompatibility evaluation
???	???
???	???
???	???
???	???
???	???

Special Controls (Class II)

- Special controls are legal requirements for all devices in the regulation and are written into the new classification regulation
- Special controls include, and are not limited to:
  - Non-clinical (analytical) validation requirements
  - Clinical validation requirements
  - Labeling requirements
  - Some postmarket requirements
- **The De Novo device must meet its own special controls**

When a De Novo Is Granted

- New device may be legally marketed
  - Subject to applicable requirements
- New classification regulation is established
- New device may be used as a predicate device for similar devices to be cleared via 510(k)
- FDA publishes Decision Summary
- FDA publishes new regulation in the Code of Federal Regulations (CFR)

GSP Neonatal Creatine Kinase – MM Kit (DEN180056)

- Number: *21 CFR 862.1506*
- Name: *Muscular dystrophy newborn screening test*
- Identification: *A muscular dystrophy newborn screening test is intended to measure creatine kinase levels obtained from dried blood spot specimens on filter paper from newborns as an aid in screening newborns for muscular dystrophy.*

GSP Neonatal Creatine Kinase – MM Kit (DEN180056)

1. Design verification and validation must include a clinical validation study that includes the following:

   (i) Results that demonstrate that the analyte being measured identifies a population of newborns who should be subject to follow up diagnostic testing for the condition being screened.

   (ii) Predictive value of the device demonstrated using either well characterized prospectively or retrospectively obtained clinical specimens from the intended use population.

   (iii) Testing performed by device users who are representative of the types of operators intended to use the test.

   (iv) A design that assesses the effects of sample collection and processing steps on test performance.

   (v) Tested confirmed positive specimens must have associated diagnostic outcome information based on confirmatory diagnostic methods, or clinically meaningful information regarding the status of the subject must be obtained.

   (vi) Data, provided or referenced, generated in samples from the intended use population, that demonstrates the upper reference interval(s), including sufficient samples to calculate the 97.5th and 99.5th percentile information, for the analyte or analytes measured by the device.

Panel Questions in Context

- FDA is asking questions today about the benefits and risks of the AvertD device.
- FDA will use your input in establishing a regulatory framework for ensuring the safety and effectiveness of similar devices yet to come:
  - Clinical validation requirements
  - Analytical validation requirements
  - Labeling requirements
  - Postmarket study requirements, if any


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