Replacement Reagent and Instrument Family Policy

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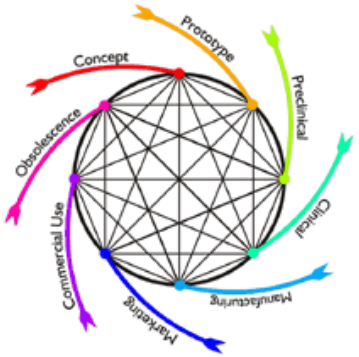

The Office of In Vitro Diagnostic Device Evaluation and Safety (OIVD)

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RR-Policy

- Well characterized clinical laboratory testing systems intended for use by ***clinical laboratory professionals***.
- Previously ***cleared*** instruments and reagents, when a claim is made for a ***new reagent/instrument*** combination.
- Introduction of ***new instrument family members*** of a previously ***cleared*** instrument family.

RR-Policy

- Based on Cleared Performance
  - evaluate your modified device against ***predefined acceptance criteria,***
  - using ***validation protocols***,
  - that were used in obtaining ***original clearance.***

RR-Policy

- The policy relies on "***Deciding When to Submit a 510(k)*** for a Change to an Existing Device", and
- Provides recommendations on the types of documentation that should be ***kept on file at your facility***.

Validation Protocols

- Method comparison, precision, reportable range; etc…

STUDY TYPES

PARAMETER	ORIGINAL SUBMISSION	ADDITIONAL REAGENTS	ACCEPTANCE CRITERIA
Method comparison	Comparative data based on scientifically valid protocols and statistically sound data assessment, see *NCCLS EP09-A2 Method Comparison and Bias Estimation Using Patient Samples*	Same studies in which N is the original 510(k).	Statistically Equivalent to Acceptance Criteria in the original 510(k) in order to maintain clearance performance
Precision	Total and within run imprecision data based on scientifically valid protocols and sound data assessment, see *NCCLS EP05-A Evaluation of Precision Performance of Clinical Chemistry Devices*	Same	Same
Sensitivity	Analytical, functional, relative, clinical sensitivity, as appropriate.	Same	Same
Reportable Range	Dynamic range data based on scientifically valid see *NCCLS EP06-A Evaluation of the Linearity of Quantitative Analytical Methods*	Same	Same
Specificity	Clinical and analytical, as appropriate Interference/cross-reactivity study , see *NCCLS EP07-A Interference Testing in Clinical Chemistry*	Same	Same
Reference Ranges	Where appropriate, reference range data based on scientifically valid protocols, see *NCCLS C28-A2 How to Define and Determine Reference Intervals in the Clinical Laboratory*	Where appropriate, reference range data including demographic data based on scientifically valid protocols	

Validation Protocols

- You should collect these data prior to marketing each new combination, and
- Maintain appropriate records at the site performing the validation.
- 21CFR Part 820.180 (Subpart M-Records)

REAGENTS

- **REAGENTS -** necessary substances that produce reactions allowing an analyte to be measured.
  - Changes to calibrator or quality control material involving the addition of **new analytes require 510(k)**
- **GENERIC reagents -** are intended to be used manually, or with any open system.
  - Laboratories assume full responsibility for performance validation.

REAGENTS

- **OEM reagents** - Analyzer manufacturer's reagents specifically for their analyzers.

- **REPLACEMENT reagents** - Generic reagents produced for use with specified analyzers by suppliers other than an OEM supplier.
  - Replacement reagents may be marketed and labeled for one specific analyzer or may claim multiple analyzers.

ANALYZERS

- **Closed Systems** - analyzers and OEM reagents provided by the same manufacturer and are configured only to be used in combination with each other.
- **Open Systems** - analyzers manufactured with general-purpose features for use only with "replacement or generic reagents".
- **Partially Closed System** - is a combination of the above.

ANALYZERS

- **Instrument Family** - consists of analyzers made by one manufacturer that yield the same analytic result from samples of the same specimen within stated tolerance limits:
  - design specifications and performance characteristics sharing a common Design History File (DHF)
  - Intended use and function
  - Device classification and product code.

ANALYZERS

- **New instrument family member** - is an instrument that has a modification to any instrument family member in either the hardware or software, but not a change in analytical technology and underlying specifications.
- The instrument should fit within the above definition of instrument family.

LABELING

- **Operator Manual** - labeling accompanying instrument for operating instructions.
- **Package Insert** - reagent labeling which may give instructions and also refer to an operator manual for detailed instruction.
- **Application Sheet** – typically contains analyzer settings, volumes, and parameters to assist laboratories in implementing use of secondary reagents with a specified open analyzer system.

OTHER DEFINITIONS

- **Test System -** is comprised of all test components required to perform an in vitro diagnostic test, i.e. clinical laboratory analyzer, reagents, calibrators and controls.
- **High Risk Device** - IVDs can be high risk to the extent that information from the device generates a misdiagnosis that may result in significant morbidity or mortality.

Clarifications

- **Class I instruments** –Class I devices such as many of these analyzers, are exempt from 510(k).
- **Combination Devices -** "Guidance on the CDRH Premarket Notification Review Program 6/30/86 – Blue Book Memo (K86-3)" http://www.fda.gov/cdrh/k863.html.

Replacement Reagent Policy

- Consult with the appropriate Division Director for assays that could have serious health risks associated with their use.
- **SPECIAL 510(k**) – like the Special 510k the RR-Policy is intended to meet predetermined criteria.
- Use the **Traditional** 510(k), when the test system does not meet acceptance criteria of the validation protocol, use a cleared predicate.

CLIA Categorization

- State you followed the rr-policy and met predetermined acceptance criteria, include labeling in sufficient detail to determine categorization.
  - Replacement reagents require a package insert and application sheet.
  - State “the labeling has not change other than instrument related information”
  - We review QC… for follow Fed, State and local…

CLIA Categorization

- ***New family member***
  - instructions for use such as an abbreviated operators manual or
  - title page that includes trade name…. and TOC
  - Side by side instrument specifications
  - list of all assays with k-numbers
  - Bundling assays provide spreadsheet in specific format… call or e-mail me or Carol

Replacement Reagent Policy

- **The RR-policy did not and does not apply to:**
  - class III devices,
  - exempt general purpose reagents
  - devices intended for use in support of blood banking practices
  - systems intended for over-the-counter (OTC) use,
  - systems intended for prescription home use,

Replacement Reagent Policy

- **The RR-policy did not and does not apply to:**
  - devices intended for point of care (POC) use… including **Physician Office Labs** (POL),
  - if specified as not applicable in **special controls**,
  - changes in the intended use of a cleared product, or….
  - e-mail when in doubt

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