Deciding When To Submit a 510(k) for a Change to an Existing Device

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Background-1

- **New guidance released August 8, 2016; we** are now in 90-day comment period *http://www.fda.gov/downloads/medicaldevices/deviceregulationandguidance/guidancedocuments/ucm514771.pdf*
- **Policy for changes to existing 510(k)s bubbles up every few years.**
  - There have even been suggestions to abolish the 510(k) program

Background-2

- Once new guidance finalized, the January 10, 1997 guidance will become obsolete.
- Policy applies only to a change to your own device.
- What triggers a change?- 2 conditions
  - *Condition 1: a major change or modification in the intended use of the device.* This is fairly non-ambiguous

Background-3

- *Condition 2: a change or modification in the device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process.* This is more ambiguous.

Major Elements of New Guidance

- **Primary elements still the same:**
  - Need new 510(k) for major change
  - May need new 510(k) for a recall
  - Still use of flow charts
- **Biggest differences:**
  - Specific reliance on QSR
  - Risk based assessments

Major Elements (#2)

- **Two step process-** the manufacturer should first conduct a risk-based assessment to ascertain if the change could significantly affect the device's safety or effectiveness, *either positively or negatively* (emphasis added).
  - This risk-based assessment should identify and analyze all new risks and changes in known risks resulting from the modification, and lead to an initial decision whether or not a new 510(k) is required.

- If the initial decision following the risk assessment is that a new 510(k) is not required, this decision should be confirmed by successful, routine verification and validation activities. If routine verification and validation activities produce any unexpected issues, any prior decision that a new 510(k) is not required should be reconsidered.

Major Elements (#3)

- **Should consider accumulation of prior changes to an existing cleared 510(k)- concept of "catch-up 510(k)"**
  - If going this route, capture all changes, even those that did not warrant a new filing.
  - If a warning has been modified, disclose this change, even if that change is not the trigger for the new 510(k).

Flow Charts- general

- **Retained Flow Chart Schemes**
  - Main Chart- types of changes
  - Chart A- labeling changes
  - Chart B- technology, engineering, performance
  - Chart C- materials changes
  - Chart D- IVDs: technology, engineering, performance, and materials
  - Charts B and C are applicable to non-IVDs and Chart D is applicable to only IVDs

Flow Chart Recaps and Summaries

- Main flow chart identifies the type of change(s), and therefore the applicable flow charts A-D.
- Chart A
  - Cannot change the intended use,
  - Generally can add a contraindication, but cannot remove one
  - Most other labeling changes are “documentation”
- First question for Charts B and C, “is this an IVD?”

Focus on Chart D- (IVDs)

- **4 Conditions Point to a New 510(k)**
  - Change in operating principle
  - Change in device-specific guidance or classification regulation
  - Based on the risk assessment of the changed device, new risks or significantly modified existing risks are identified. [pre-validation]
  - Design verification and validation activities produced unexpected issues of safety or effectiveness. [post-validation]

Changes in IVD Technology-1

- **Examples *Likely* to Affect Technology**
  - Liquid to solid reagent
  - changes from radioimmunoassays (RIA) to non-RIAs
  - changes in the antibody
  - changes in detection reagents
  - changes in critical reaction components
  - changes in conjugates

Changes in IVD Technology-2

- **Examples that *May* Affect Technology**
  - changes in calibration materials and quality control materials (affect claimed cutoff?)
  - changes in substrates
  - changes in specimen type
  - changes in specimen processing
  - changes in incubation times and temperatures

Changes in IVD Technology-3

- **Examples that Likely Do Not Affect Technology**
  - changes to external packaging
  - changes to use a new lot or batch for the same antibody or enzyme
  - changes to a new vendor for the same reagent
  - changes in concentrations of packaged reagents, provided the same diluted concentration was used in the assay (procedural convenience?, ensure shelf life is not affected)

Change Identified in a Device-Specific Guidance or Classification Regulation

- "When a device-specific guidance identifies a change that FDA has determined could significantly affect safety or effectiveness, a new 510(k) is generally required under 21 CFR 807.81(a)(3)(i). *A change or modification in the device that could significantly affect the safety or effectiveness of the device, e.g., a significant change or modification in design, material, chemical composition, energy source, or manufacturing process.*

Additionally, in the case of some IVDs, FDA has established specific requirements (e.g., special controls) that are identified in the classification regulation."

Risk Assessment Identifies New Risk

- **Consult Section E of FDA Guidance**
  - Basic principles of risk management, recommend ISO 14971
  - Relationship between hazards and harm
  - Pay extra attention to performance around cutoffs
  - Human factors may have a role

Verification and/or Validation Activities Produced Unexpected Issues of Safety or Effectiveness?

- A new 510(k) is likely not required where (1) standard methods and established criteria (e.g., clinically appropriate criteria or criteria justified by relevant development data, as applicable) are used to verify and validate the modification, (2) the results of verification and validation indicate that the performance is within the criteria, (3) the performance of the modified IVD has not significantly changed from the previously cleared performance claims.

Guidance Includes ~20 Pages of IVD Examples

- Examples cover each type of change
  - Labeling, technology, engineering, performance, and materials.
  - As stated, all changes are vetted through risk assessment

Documentation Option-1

Most Elements of a Change Order

- Product name
- Date of modification assessment
- Description of the device
- Description of the modification(s)
- Reason why the modification(s) is being made
- Applicable regulatory history, including the 510(k) number of the last cleared version of the device

Documentation Option-2

- Comparison of the modified device to the last cleared version of the device (consider including a table, like an SE table for a 510(k))
- Applicable elements of this guidance, including the applicable questions from the body of the document
- Analysis and assessment of the elements on this list and a conclusion of whether a new 510(k) is required
- Reference to related documents, particularly those that support the decision whether or not a new 510(k) is required (e.g., risk analysis)
- Signature(s)

Questions