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510(k)s for Changes to Devices – What We Know and Do Not Know

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Unnecessary 510(k)s are Submitted

- Company needs
  - Certainty
    - Specific change is in a gray area
    - Cited for failure to submit a 510(k) in the past
    - Risk mitigation for changes implemented without FDA authorization
  - Documentation of FDA market authorization
    - Strategic considerations; establishment of a predicate device
    - Promotion , advertising and sales – despite 21 CFR § 807.97
    - Import and export reasons
    - Reimbursement
- FDA ignores 21 CFR § 807.100(a)(5)

(5) Advise the applicant that the premarket notification is not required.

Consequences of Unnecessary 510(k)s

- FDA review diverts resources from matters of greater public health importance
- Unnecessary 510(k)s generate unnecessary 510(k)s
- Can result in regulatory vulnerability
  - 510(k) submissions for marketed devices (e.g., "catch-up 510(k)s") can lead to compliance actions and market withdrawal
  - 21 CFR § 807.100 - "Until the applicant receives an order declaring a device substantially equivalent, the applicant may not proceed to market the device."
  - "AI" and "NSE" letter say not to market!

Requirements for Non-Exempt Devices

- 21 CFR § 807.81(a)(3) describes circumstances in which a 510(k) is required for a device change or modification
  - Scope
    - Persons required to register that has a device
      (1) currently in commercial distribution; or
      (2) to be re-introduced into commercial distribution
  - Device is about to be significantly changed or modified in
    - Design
    - Components
    - Method of manufacture
    - Intended use

Requirements (continued)

- What is a significant change or modification?
  - Could significantly affect the safety or effectiveness of the device
    - Design
    - Material
    - Chemical composition
    - Energy source
    - Manufacturing process
    - A major change or modification in intended use
  - Major change or modification in the intended use of the device
- FDA expectations communicated via guidance document

Know the Exemptions

- General exemptions
  - 21 CFR § 807.20(c) – Registration and listing
  - 21 CFR § 807.65 - Registration
  - 21 CFR § 807.85 – Premarket notification
- Device -type specific exemptions
  - 21 CFR § 862-892
  - Limitations of exemptions from section 510(k) found in 21 CFR § XXX.9

Exemptions from 510(k)

- General exemptions

  807.20(c) – Exemptions from registration and listing

  (c) Registration and listing requirements shall not pertain to any person who:

  (1) Manufacturers devices for another party who both initiated the specifications and commercially distributes the device;

  (2) Sterilizes devices on a contract basis for other registered facilities who commercially distribute the devices.

  (3) Acts as a wholesale distributor, as defined in 807.3(s), and who does not manufacture, repackage, process, or relabel a device.

General Exemptions (continued)

807.65 – Exemptions from registration

(a) … raw materials or components to be used in the manufacture or assembly of a device …

(b) … devices to be used solely for veterinary purposes.

(c) … general purpose articles …

(d) … practitioners … who manufacture or otherwise alter devices solely for use in their practice.

(e) … retail establishments making final delivery or sale to the ultimate user. [including private label distribution]

(f) … devices solely for use in research, teaching, or analysis …

(h) Carriers by reason of their receipt, carriage, holding or delivery of devices …

(i) Persons who dispense devices … or … render a service necessary to provide the consumer … with a device or the benefits to be derived from the use of a device …

General Exemptions (continued)

807.85 – Exemptions from premarket notification

(a) A device is exempt … if the device intended for introduction into commercial distribution is not generally available in finished form for purchase and is not offered through labeling or advertising … for commercial distribution, and the device meets one of the following conditions:

(1) It is intended for use by a patient named in the order of the physician or dentist (or other specially qualified person); or

(2) It is intended solely for use by a physician or dentist (or other specially qualified person) and is not generally available to, or generally used by, other physicians or dentists (or other specially qualified persons).

(b) A distributor who places a device into commercial distribution for the first time under his own name and a repackager who places his own name on a device and does not change any other labeling or otherwise affect the device shall be exempted from the premarket notification requirements of this subpart if:

(1) The device was in commercial distribution before May 28, 1976; or

(2) A premarket notification submission was filed by another person.

Device Type Specific Exemptions

21 CFR 862-892

- Most class I devices
- Select class II devices
- Subject to limitations “21 CFR XXX.9” and any device specific limitations
- Examples:
  - Sec. 880.5090 Liquid bandage – class I exempt, only as a skin protectant
  - Sec. 890.5740 Powered heating pad – class II exempt
  - Sec. 874.1050 Audiometer – class II, exempt if it complies with A.N.S.I. S3.6-1996, "Specification for Audiometers"

Limitations of "Device -Type" Exemptions

(a) The device is intended for a use different from the intended use of **a legally marketed device in that generic type of device**; e.g., the device is intended for a different medical purpose, or the device is intended for lay use where the former intended use was by health care professionals only;

(b) The modified device operates using a different fundamental scientific technology than **a legally marketed device in that generic type of device**; e.g., a surgical instrument cuts tissue with a laser beam rather than with a sharpened metal blade, or an in vitro diagnostic device detects or identifies infectious agents by using deoxyribonucleic acid (DNA) probe or nucleic acid hybridization technology rather than culture or immunoassay technology; or

Limitations (continued)

c) The device is an in vitro device that is intended:

(1)For use in the diagnosis, monitoring, or screening of neoplastic diseases with the exception of immunohistochemical devices;

(2) For use in screening or diagnosis of familial or acquired genetic disorders, including inborn errors of metabolism;

(3) For measuring an analyte that serves as a surrogate marker for screening, diagnosis, or monitoring life-threatening diseases such as acquired immune deficiency syndrome (AIDS), chronic or active hepatitis, tuberculosis, or myocardial infarction or to monitor therapy;

(4) For assessing the risk of cardiovascular diseases;

(5) For use in diabetes management;

(6) For identifying or inferring the identity of a microorganism directly from clinical material;

(7) For detection of antibodies to microorganisms other than immunoglobulin G (IgG) or IgG assays when the results are not qualitative, or are used to determine immunity, or the assay is intended for use in matrices other than serum or plasma;

(8) For noninvasive testing as defined in § 812.3(k) of this chapter; and

(9) For near patient testing (point of care).

Often Overlooked Facts

- Changes to devices subject to the general 510(k) exemptions are not subject to ".9" limitations
- 510(k) clearances for certain changes that exceed the ".9" limitations expand the exemption, specifically;
  - changes in intended use; and
  - changes in fundamental scientific technology
- Combination devices, i.e., devices comprised of class I, II or III devices, and "bundled" devices
  - Are generally "classified" in the highest classification
  - Does not mean that the change rules applicable to a lower classification do not apply

In regard to the guidance on 21 CFR § 807.81(a)(3), what will FDA do?

Answer

I do not know … but my bet is more 510(k)s will be required.

Closing Thoughts

- As per the preamble to 21 CFR § 807, FDA "believes that the manufacturer is the person best qualified to make this determination"
  - But FDA administratively has last word
    - Therefore, all decisions must be documented in anticipation of an FDA inspection
- Not every change requires a 510(k), therefore;
  - Know the many exemptions from 510(k) requirements and, for device-specific exemptions, the limitations
  - For devices that are not 510(k) exempt, follow the guidance document that reflects FDA's current interpretation of "could significantly affect the safety or effectiveness" and "major change or modification in the intended use."

Closing Thoughts

- Thoroughly understand and apply the law set forth in the regulations and the principles set forth in FDA's guidance even though the guidance is not binding
  - If you decide a new 510(k) is not required, reasoning must be thorough, supported by sound arguments/data, and documented
  - After documenting change with a thorough narrative, attach flow chart documentation