

510(k) Program AMDM/FDA-OIVD Submissions Workshop April 17, 2012



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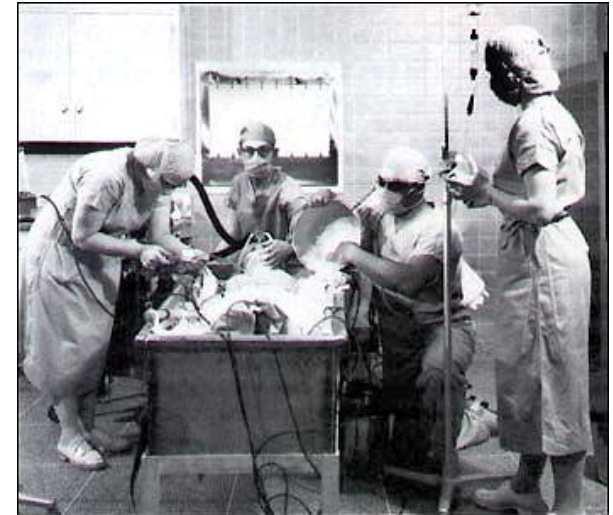
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The 510(k) program was established more than 30 years ago

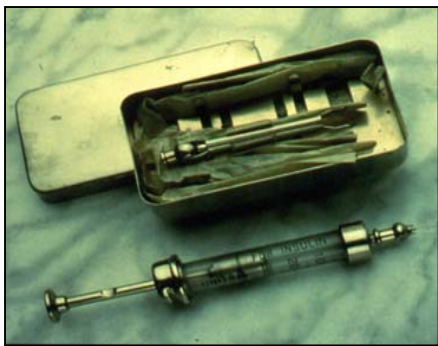
- Introduced as part of the Medical Device Amendments to the Federal Food, Drug, and Cosmetic Act in 1976
- Devices were much simpler
 - The electronics revolution and trend towards miniaturization had not yet begun
 - There was no Internet
 - There were few combination products





Much has changed over time...

■ In devices themselves...



Yesterday

- Simple barrel, rod, plunger devices



Today

- Mechanical systems reduce needle sticks
- Retractable needles
- Projectile rigid cover

... and in device regulation.



“The Poison Squad”



Harvey Washington Wiley, M.D., (third from right) and the Division of Chemistry Staff in 1883



Federal Food and Drugs Act of 1906 (The “Wiley Act”)



U.S. Food and Drug Administration



Department of
Health and
Human Services

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FEDERAL FOOD AND DRUGS ACT OF 1906 (THE “WILEY ACT”)

PUBLIC LAW NUMBER 59-384

34 STAT. 768 (1906)

21 U.S.C. Sec 1-15 (1934)

(REPEALED IN 1938 BY 21 U.S.C. Sec 329 (a))

TABLE OF CONTENTS

FEDERAL FOOD AND DRUGS ACT OF 1906

TITLE 21--FOOD AND DRUGS

CHAPTER 1--ADULTERATED OR MISBRANDED FOODS OR DRUGS

SUBCHAPTER I--FEDERAL FOOD AND DRUGS ACT OF 1906



Federal Food, Drug, and Cosmetic Act

■ 1938

- President Roosevelt signed the Food, Drug, and Cosmetic Act which superseded the “Wiley Act”, and introduced “safety” as criterion for premarket approvals of drugs.

■ 1962

- “Effectiveness” was added.





FDA Undercover

- **Illegal sales of amphetamines and barbiturates occupied more regulatory concern at FDA than all other drug problems combined from the 1940s to the 1960s. Interdiction in some venues required undercover tactics, as indicated here by these two inspectors posing as truck drivers.**





Medical Device Amendments of 1976

- Enacted on May 28, 1976, to ensure safety and effectiveness of medical devices, including diagnostic products
 - Some products must have premarket approval by FDA; others must meet performance standards prior to marketing.
- Defined a device (201(h) of the Act)
- Required risk-based classification of devices



Pre- vs. Post-Amendment Devices

- MDA divided medical devices based on when they were introduced into commercial distribution*:
 - Pre-amendment devices (pre-May 28, 1976)
 - Post-amendment devices (post-May 28, 1976)

*Commercial distribution and Pre-amendment Status are determined by CDRH's Office of Compliance.

(<http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/ComplianceActivities/ucm072746.htm>)



Device Classification

- As per section 513 of FFD&C Act, FDA classified all legally marketed pre-amendment devices by generic type.
- Device Type – 21 CFR 860.3(i)
 - Generic type of device means a grouping of devices that do not differ significantly in purpose, design, materials, energy source, function, or any other feature related to safety and effectiveness, and for which similar regulatory controls are sufficient to provide reasonable assurance of safety and effectiveness.



Device Classification – Based on Risk

- Section 513(a)(2) of the FFD&C Act requires FDA to determine safety and effectiveness of a device by weighing any probable benefit to health from the use of the device against any probable risk of injury or illness from the use.



Regulatory Classes: I, II, and III

- **Three regulatory Classes – based on the level of control necessary to provide reasonable assurance of safety and effectiveness:**
 - **Class I – General Controls**
 - **Class II – General Controls & Special Controls**
 - **Class III – General Controls and Premarket Approval**



Description of Classes I, II, and III

■ Class I:

1. **Devices for which general controls and special controls are insufficient to provide reasonable assurance the safety and effectiveness of such devices, but devices:**
 - **are not life-sustaining or life-supporting;**
 - **are not of substantial importance in preventing impairment of human health; and**
 - **do not present a potential unreasonable risk of illness or injury; and**
2. **Devices for which general controls are sufficient to provide reasonable assurance of the safety and effectiveness of such devices.**



Description of Classes I, II, and III

- **General Controls include:**
 - Prohibition against adulterated or misbranded devices
 - Premarket notification (510(k)) requirements
 - Banned devices
 - Good Manufacturing Practices
 - Registration of manufacturing facilities
 - Listing of device types
 - Record keeping
 - Repair, replacement, refund



Description of Classes I, II, and III

■ Class II:

1. Devices which cannot be classified into Class I because general controls by themselves are insufficient to provide reasonable assurance of the safety and effectiveness of such devices, but...
2. For which there is sufficient information to establish special controls to provide such assurance.



Description of Classes I, II, and III

- **Special Controls include:**
 - Guidance
 - Performance standards
 - Discretionary, voluntary national or international standard, recognized by rulemaking
 - Postmarket surveillance
 - Patient registries
 - Other



Description of Classes I, II and III

■ Class III:

1. **Devices for which insufficient information exists to determine that general and special controls are sufficient to provide reasonable assurance of the safety and effectiveness of such devices; and**
2. **Such devices:**
 - **Are life-sustaining or life-supporting;**
 - **Are of substantial importance in preventing impairment of human health; or**
 - **Present unreasonable risk of illness or injury.**



Classification Regulations

- Classification regulations describe the device type as it existed prior to May 28, 1976
- New uses or technologies may be found through the product codes.



Classification of Post-Amendment Devices

■ **Section 510(k) of FFD&C Act:**

Each person who is required to register under this section and who proposes to begin the introduction or delivery for introduction into interstate commerce for commercial distribution of a device intended for human use shall, at least ninety days before making such introduction or delivery, report to the Secretary or person who is accredited under section 523(a) (in such form and manner as the Secretary shall by regulation prescribe)—

- (1) the class in which the device is classified under section 513 or if such person determines that the device is not classified under such section, a statement of that determination and the basis for such person's determination that the device is or is not so classified, and**
- (2) action taken by such person to comply with requirements under section 514 or 515 which are applicable to the device.**



Classification of Post-Amendment Devices

- The 510(k) process is used to classify individual post-amendment devices:
 - Either find a device substantially equivalent to a predicate; or
 - Find a new device that must be placed automatically into class III and require PMA, de novo, or reclassification before marketing in U.S.



Classification Regulations

Classification regulations for individual device types found in 21 CFR Parts 862-892

Example:

PART 870 -- CARDIOVASCULAR DEVICES

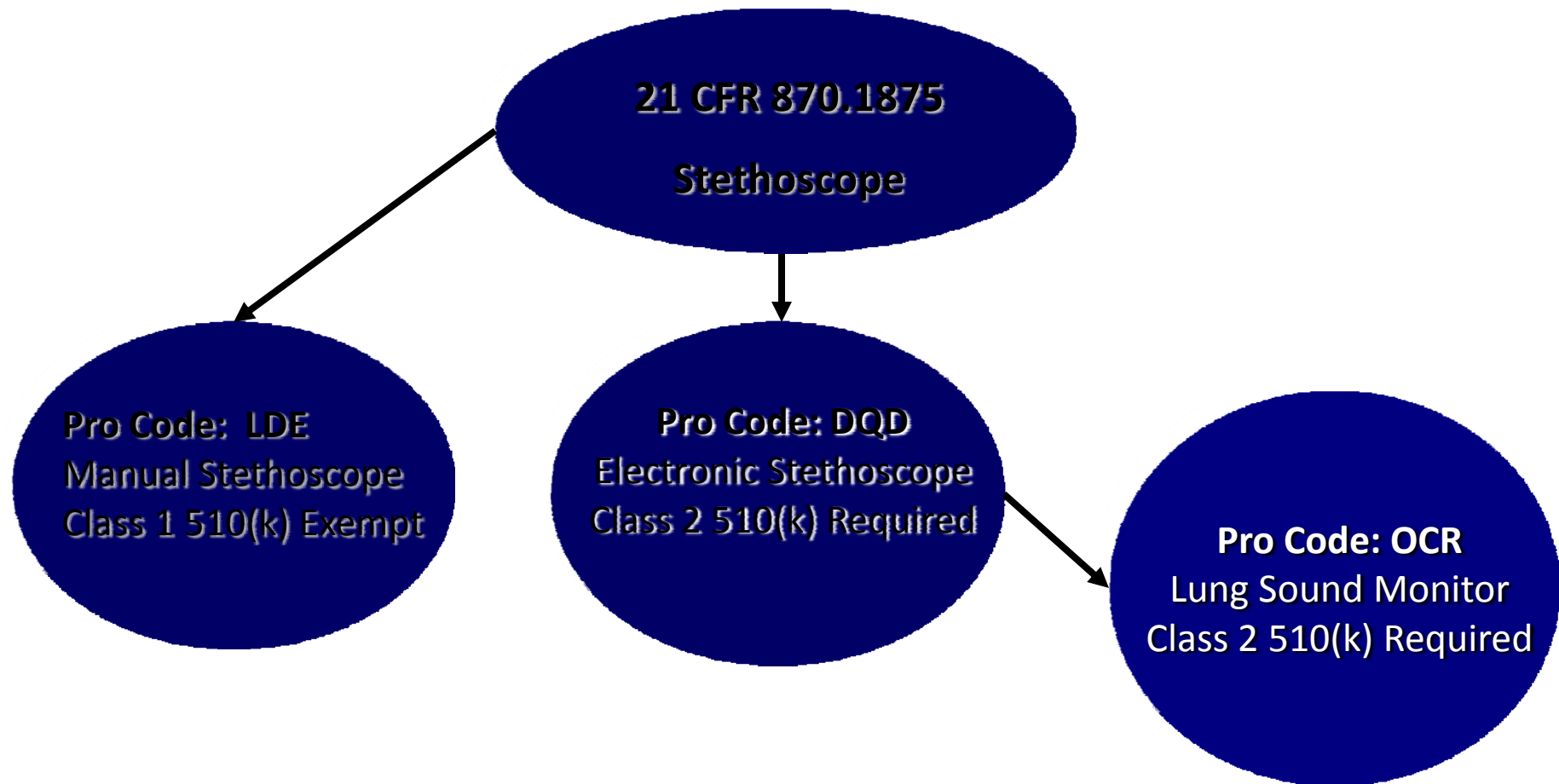
Regulation 870.1875

Stethoscope.

- (a) **Manual stethoscope** --(1)*Identification*. A manual stethoscope is a mechanical device used to project the sounds associated with the heart, arteries, and veins and other internal organs. (2)*Classification*. **Class I** (general controls). The device is exempt from the premarket notification procedures in subpart E of part 807 of this chapter subject to the limitations in 870.9.
- (b) **Electronic stethoscope** --(1)*Identification*. An electronic stethoscope is an electrically amplified device used to project the sounds associated with the heart, arteries, and veins and other internal organs. (2)*Classification*. **Class II** (performance standards).



Classification Regulations & Product Codes





Why 510(k)?

- The 510(k) process is meant to:
 - Classify post amendment* devices
 - Find a device substantially equivalent; or
 - Find a new device not substantially equivalent automatically placing device type into class III resulting in:
 - Requirement for PMA;
 - Eligibility for de novo; or
 - Requiring reclassification before marketing

****Post amendment – Post May 28, 1976 Medical Device Amendments to FF,D,&C Act***



What is Substantial Equivalence?

■ 1976 Congressional Record

“The term ‘substantially equivalent’ is not intended to be so narrow as to refer only to devices that are identical to marketed devices nor so broad as to refer to devices which are intended to be used for the same purposes as marketed products. The committee believes that the term should be construed narrowly where necessary to assure the safety and effectiveness of a device but not narrowly where differences between a new device and a marketed device do not relate to safety and effectiveness.”



What is a Predicate?

■ 21 CFR Part 807.92(a)(3)*

An identification of the legally marketed device to which the submitter claims equivalence. A legally marketed device to which a new device may be compared for a determination regarding substantial equivalence is a device that was legally marketed prior to May 28, 1976, or a device which has been reclassified from class III to class II or I (the predicate), or a device which has been found to be substantially equivalent through the 510(k) premarket notification process.

***Regulation written in 1990.**



So 510(k) is...

- Premarket Notification
- Section 510(k) of FFD&C Act
- 21 CFR 807 Subpart E
- Determination regarding marketing clearance
- A process that allows FDA to make a determination regarding Substantial Equivalence (SE)
- The classification process for an individual device
- 1986 Guidance on the CDRH Premarket Notification Review Program
 - <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm081383.htm>



The Premarket Notification (510(k)) Process is Used to...

- Identify new devices that must be placed automatically into class III and undergo premarket approval or reclassification before they are marketed
- For example:
 - A new device that is Not Substantially Equivalent (NSE) is in class III, whereas a new device that is Substantially Equivalent (SE) is in the same regulatory class as the device it is found equivalent to (class I or II)



A 510(k) is required when...

- **Introducing device to the market for the first time**
- **Changing a device's indications for use**
- **Making significant modification to device that could affect safety or effectiveness**



Modifications

- Changes in Indications for Use
- Modifications that could significantly enhance (or decrease) safety or effectiveness
 - E.g., change in design, materials, chemical composition, energy source, or manufacturing process
- 1997 Guidance: “Deciding When to Submit a 510(k) for Change to an Existing Device”
 - <http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm080235.htm>



510(k) Exempt Devices

- **Some device types are exempt from the 510(k) requirements of the FFD&C Act:**
 - **Pre-amendments devices (legal pre-1976)**
 - **Unfinished devices**
 - **Devices exempt by statute or regulation from 510(k)**
 - **Class I (93%), Class II (8%) subject to limitations**
 - **Finished devices not sold in U.S.**
 - **Devices covered under another 510(k), e.g., private labeled device**
 - **Custom devices**
 - **General purpose articles**
 - **Veterinary devices**



A Device Must be Compared to...

- A legally marketed device (a predicate*) that does not require a PMA, i.e.:
 - A pre-amendment device*
 - A device found by FDA to be Substantially Equivalent (SE)
 - A reclassified device*
 - A device classified by a de novo petition

***21 CFR 807.92(a)(3)**



Substantially Equivalent (SE)?

- If SE → Device may be marketed without a PMA
- If NSE → PMA, PDP, HDE application or de novo petition required



A Device is SE if...

- In comparison to a predicate device, it:
 - Has the same intended use, and
 - Has the same technological characteristics as the predicate device,

or...

(cont'd)



A Device is SE if...

- In comparison to a predicate device it:
 - Has the same intended use, and
 - Has different technological characteristics and the information in the 510(k):
 - Does not raise different questions of safety and effectiveness, and
 - Information submitted demonstrates, including appropriate clinical or scientific data, it is at least as safe and effective as the predicate
- Approximately 85% have been determined to be SE



New Technological Features

- **Technological differences may include:**
 - **Modifications in design, materials, or energy sources, for example:**
 - **changes in the power levels of electrical surgical instruments**
 - **use of new reagents in in vitro diagnostic devices**
 - **use of new materials in orthopedic implants**
 - **use of new battery designs in implanted pacemakers**



A Device is NSE if...

- There is no predicate device; or
- It has a new intended use; or
- It has different technological characteristics compared to the predicate device and it raises a different type question of safety and effectiveness; or
- It does not demonstrate that it is at least as safe and effective as the predicate.



Not Substantially Equivalent

- Approximately 3% – 4% have been determined NSE (remaining ~10% are withdrawn or not-a-device).
- Data is looked at last in the 510(k) regulatory process.
- FDA usually asks for additional information at least once prior to determining the device is NSE for lack of data.



Timeframes

- Under the Medical Device User Fee Amendments of 2007 (MDUFA), FDA is subject to the following performance goals:
 - FDA will issue a decision for 90% of 510(k) submissions within 90 days.
 - FDA will issue a decision for 98% of 510(k) submissions within 150 days.

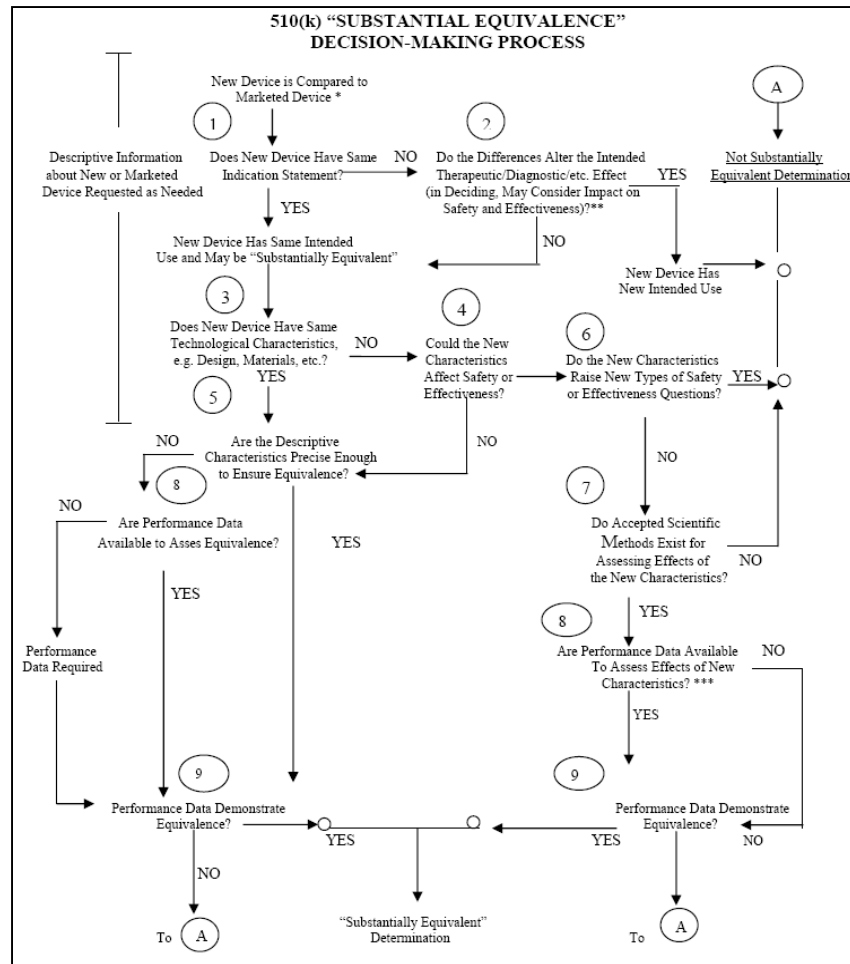


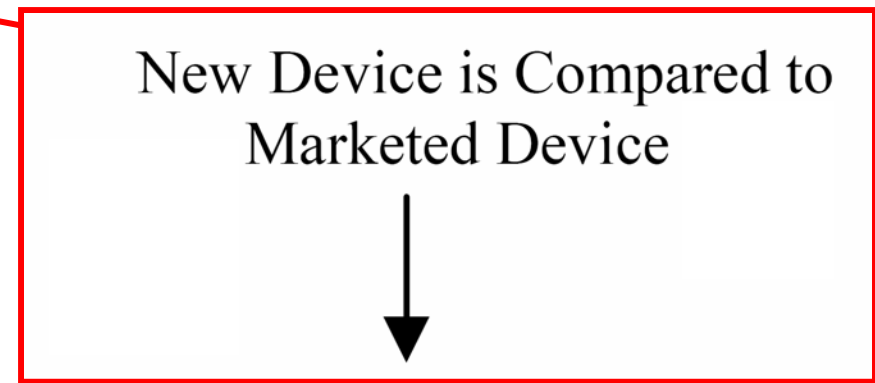
Options when Reviewing Information

- **FDA may request Additional Information (AI), if needed to make a determination.**
 - May be made by standard mail, fax, email, or phone.
- **A review may result in any of the following determinations:**
 - **Substantially Equivalent (SE)**
 - **Substantially Equivalent (SE) with Limitations**
 - **Not Substantially Equivalent (NSE)**



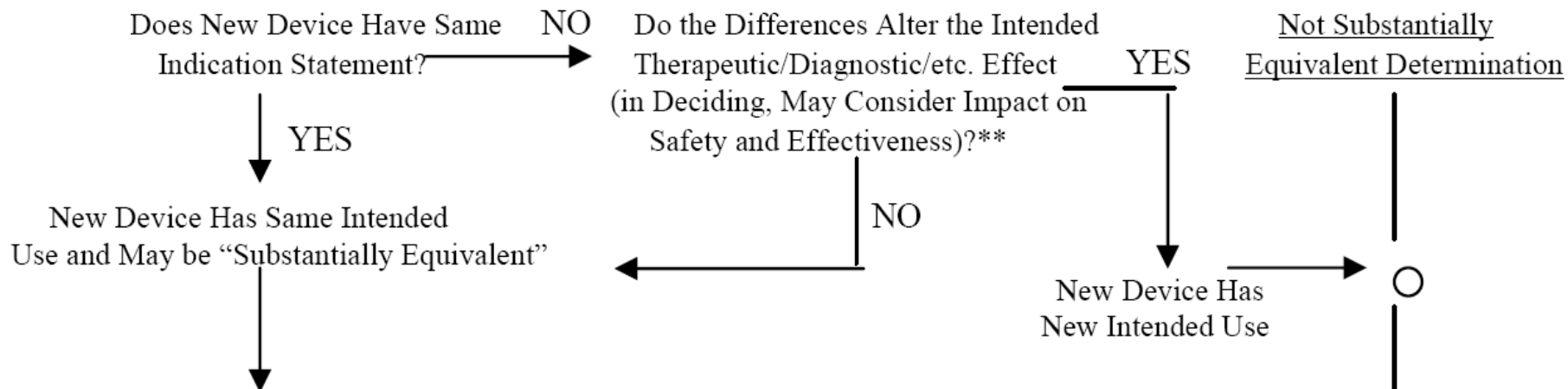
The 510(k) Flowchart: Overview





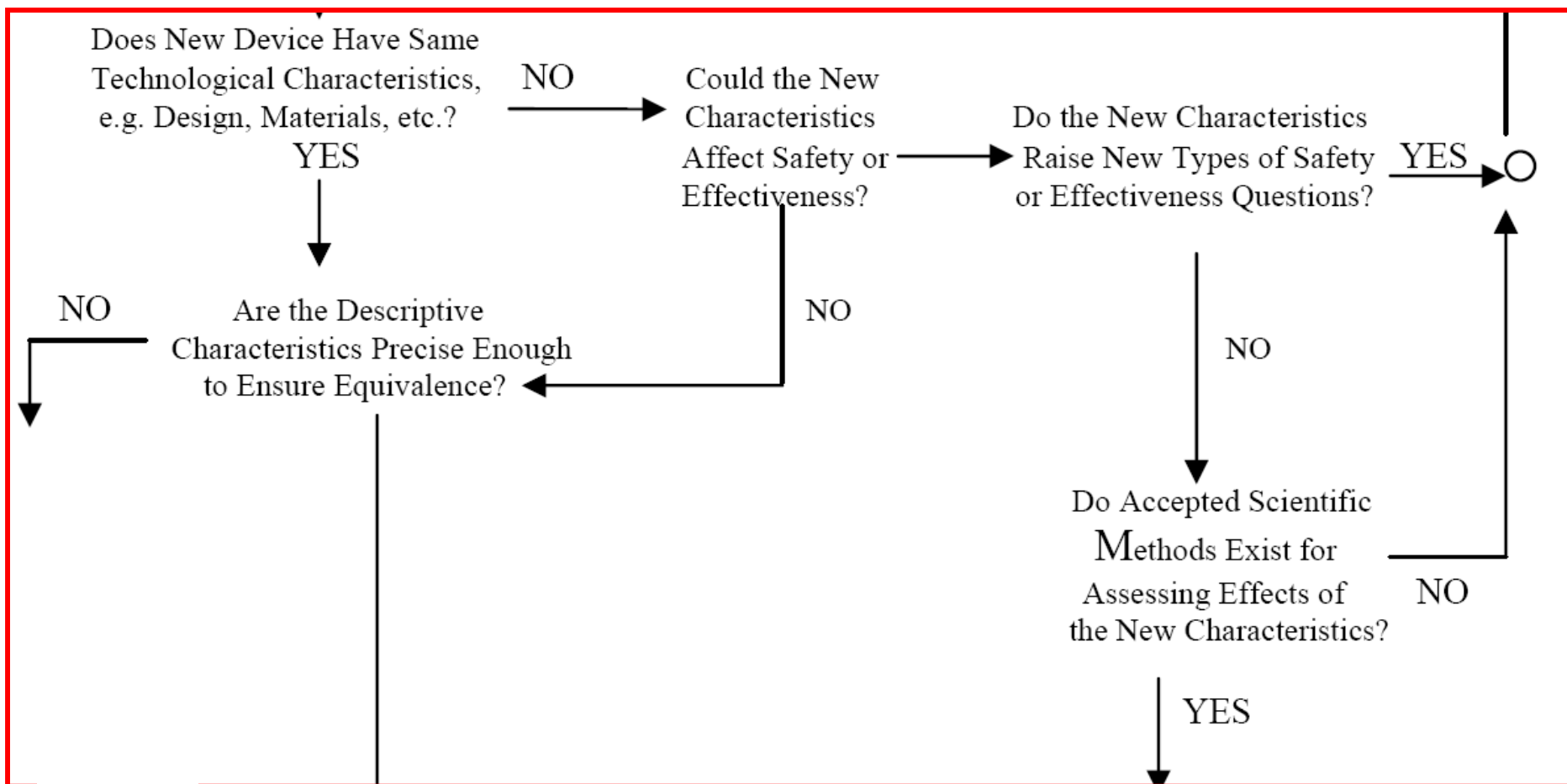


The 510(k) Flowchart: Intended Use



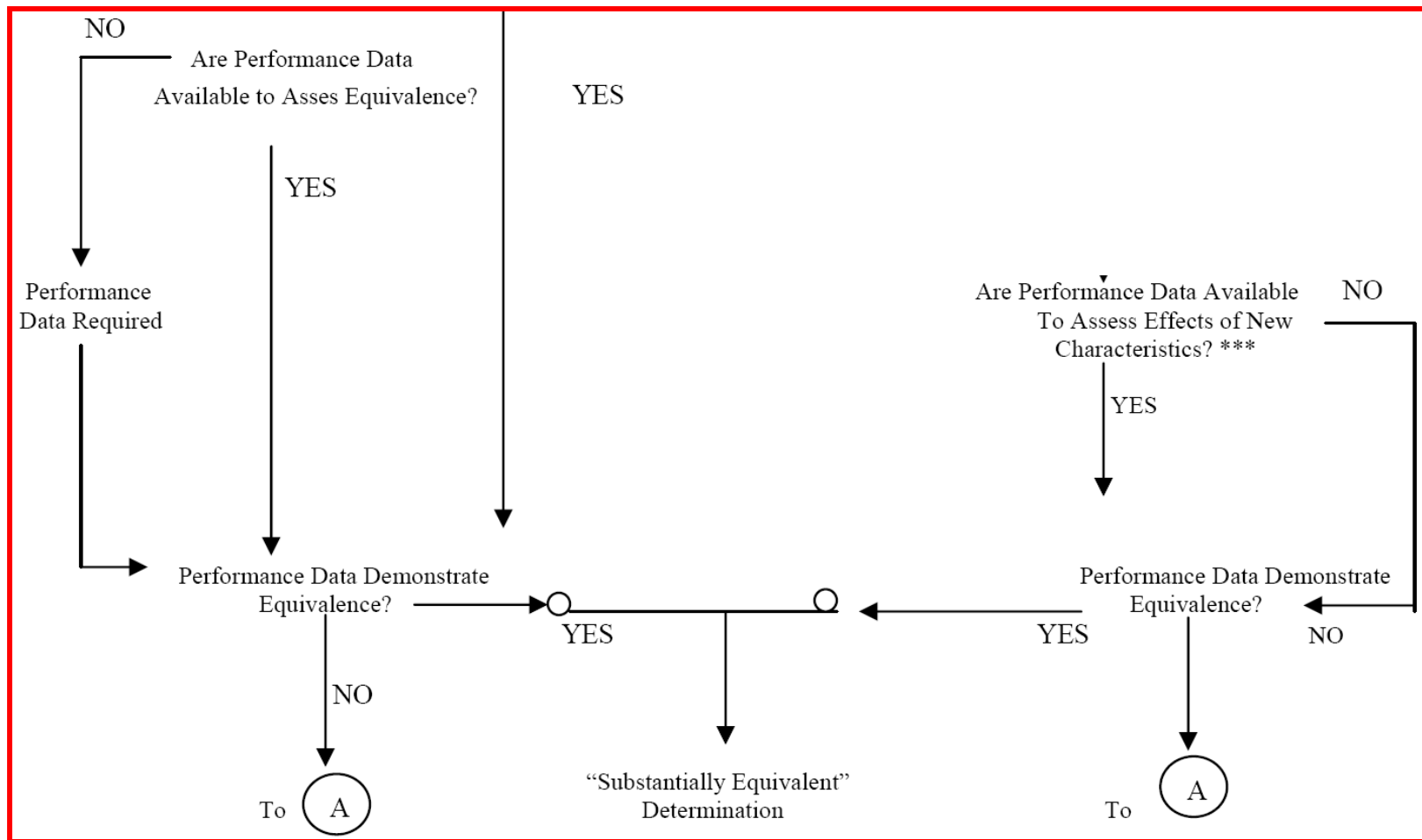


The 510(k) Flowchart: Technology





The 510(k) Flowchart: Performance





The Review

- The information requested by FDA varies based on the device type, indications for use, technology, etc.
 - Descriptive Characteristics
 - Bench Testing
 - Animal Testing
 - Clinical Studies



The Review

- **Horizontal Standards and Guidance**
 - **Biocompatibility**
 - **Sterilization**
 - **Software**
 - **Electrical Safety**
 - **Electromagnetic Compatibility**



The Review

- **Vertical Standards and Guidance**
 - **Indicates information needed for specific types of devices.**
 - **Information requested under a vertical standard or guidance may supersede that requested under a horizontal standard or guidance.**



Device-Specific Examples

- **Non-Invasive Blood Pressure Devices:**
 - Voluntary consensus standard exists
 - Clinical data are required





Device-Specific Examples

- **Pulse Oximeters:**
 - Voluntary consensus standard exists
 - Clinical data are required
 - Neonatal indications rely on adult data





Device-Specific Examples

- **Bone Plates and Screws:**
 - Voluntary consensus standard exists
 - Level of evidence required ranges:
 - Descriptive characteristics alone are sufficient (rarely)
 - Bench testing is sufficient (typically)
 - Animal or cadaver studies are required (sometimes)
 - Clinical testing is required (rarely)





510(k) Examples

■ Straight Decision

- E.g., Catheter: Original manufacturer not the original distributor now wants to be a distributor
 - 510(k) for identical device





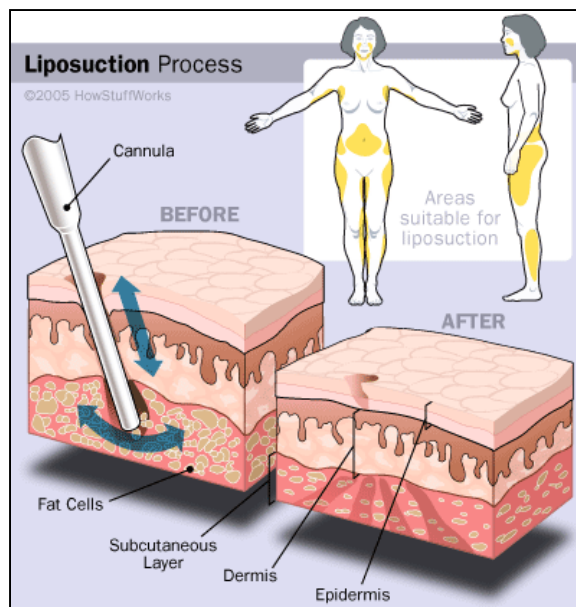
510(k) Examples

- **New Indication for Use → SAME Intended Use**
 - **E.g., Blood Access Device: Femoral to Subclavian Access**



510(k) Examples

- New Indication for Use → NEW Intended Use
- E.g., Liposuction





510(k) Examples

- New Technological → NO New Type of Question Characteristics
 - E.g., Analog to Digital





510(k) Examples

- **New Technological → NEW Type of Question Characteristics**
 - E.g., Electrosurgical device to extracorporeal shockwave lithotripsy device



Important 510(k) Content Points to Consider

Consider

■ Licensing of a 510(k)?

- A firm may not **both** manufacture and distribute a device without their own 510(k) (21 CFR 807.85(b)(2)).

■ Can you share a 510(k)? Sort of?

How? First...

- Under 21 CFR § 807.85(b) as a private label distributor or repackager of a legally marketed device
- Cannot both manufacture and distribute without your own 510(k) (21 CFR 807.85(b))
- Labeling requirements (§ 801.1(a),(c), and (e))



Summary: 510(k) Today

- **510(k) is the largest premarket program at FDA, addressing a great diversity of device types.**
- **50% of devices go to market as “510(k) exempt.” Examples: adhesive bandages, hospital beds, non-powered breast pumps – all subject to limitations on exemption.**
- **There are 3,000-4,000 510(k) submissions per year, compared to 30-50 PMA applications.**
- **The program supported in part by user fees negotiated with industry and passed by law.**



Summary: 510(k) Today

- Most 510(k)s are class II devices.
- Many significant-risk devices to go market via 510(k) route, including implants and life-sustaining and life-supporting devices.
- Approximately 8% of 510(k)s are reviewed by third parties.
- A few 510(k) submissions receive expedited review.
 - E.g., battlefield use or important for quality of life.



Summary: 510(k) Today

■ Valid Scientific Evidence

- Valid scientific evidence is required to be submitted in support of a 510(k) (21 CFR 860.7).
- Evaluation is risk-based and data-driven, focusing on indications for use, technological characteristics, and performance.
- Most 510(k) submissions include performance data (bench, animal, and/or clinical).
- Approximately 10% of 510(k)s include clinical data.



Summary: 510(k) Today

■ Premarket Tools

- Many pre-Investigational Device Exemption Applications (pre-IDEs) are for 510(k)s.
- Many IDEs are for 510(k)s.
- 510(k) reviews may include consults with other CDRH Offices such as OSEL and OSB, which together perform hundreds (500+) of 510(k) consults each year.



Summary: 510(k) Today

■ Postmarket Tools

- A manufacturer can be required to perform postmarket studies of certain class II devices cleared under 510(k).
- A manufacturer can be required to track certain class II devices cleared under 510(k).



Conclusion

- **The 510(k) Program has evolved over time through statutory and regulatory changes, as well as through guidance.**
- **The current program is large and complex – there is more than just one type of 510(k).**
- **While we should not ignore the successes it has had, the 510(k) program should continue to be periodically reviewed and re-evaluated.**



Thank You!