Glisland® Training Series:

Medical Device Submissions in the United States

Glisland, Inc.
http://www.glisland.com

Objectives

- Review medical device classification scheme and regulatory review process.
- Discuss submission methods.
- Discuss FDA review time and fees.
- Learn when to communicate with FDA regarding submissions.

Medical Device Amendments of 1976

- Devices were first regulated by FDA in 1976 under the *Medical Device Amendments*
- Before 1976, devices were subject only to the adulteration and misbranding provisions of *FD&C Act*
- The amendments:
  - Expended definition of device (e.g. to include IVD)
  - Classified devices into class I, class II ad class III
  - Established safety and efficacy requirements

Device Classification Factors

- Intended use
- Indications for use
- Risk to the patient and/or to the user

Indication for Use Vs. Intended Use

- Indication for Use: specific diagnostic or treatment uses for which the manufacturer is applying for the device.
- Intended Use: all the marketing claims made for a device, whether written or verbal, by an employee or representative of the manufacturer.
- New Intended Use is subject to a new classification and/or new submission.

Statutory and Regulatory Controls

General Controls

- Adulteration and Misbranding provisions
- Establishment registration and device listing
- Compliance with QSR
- Submission of 510(k)
- Banned devices
- Notification and Repair, replacement, and refund provisions
- Records and reports
- Restricted devices

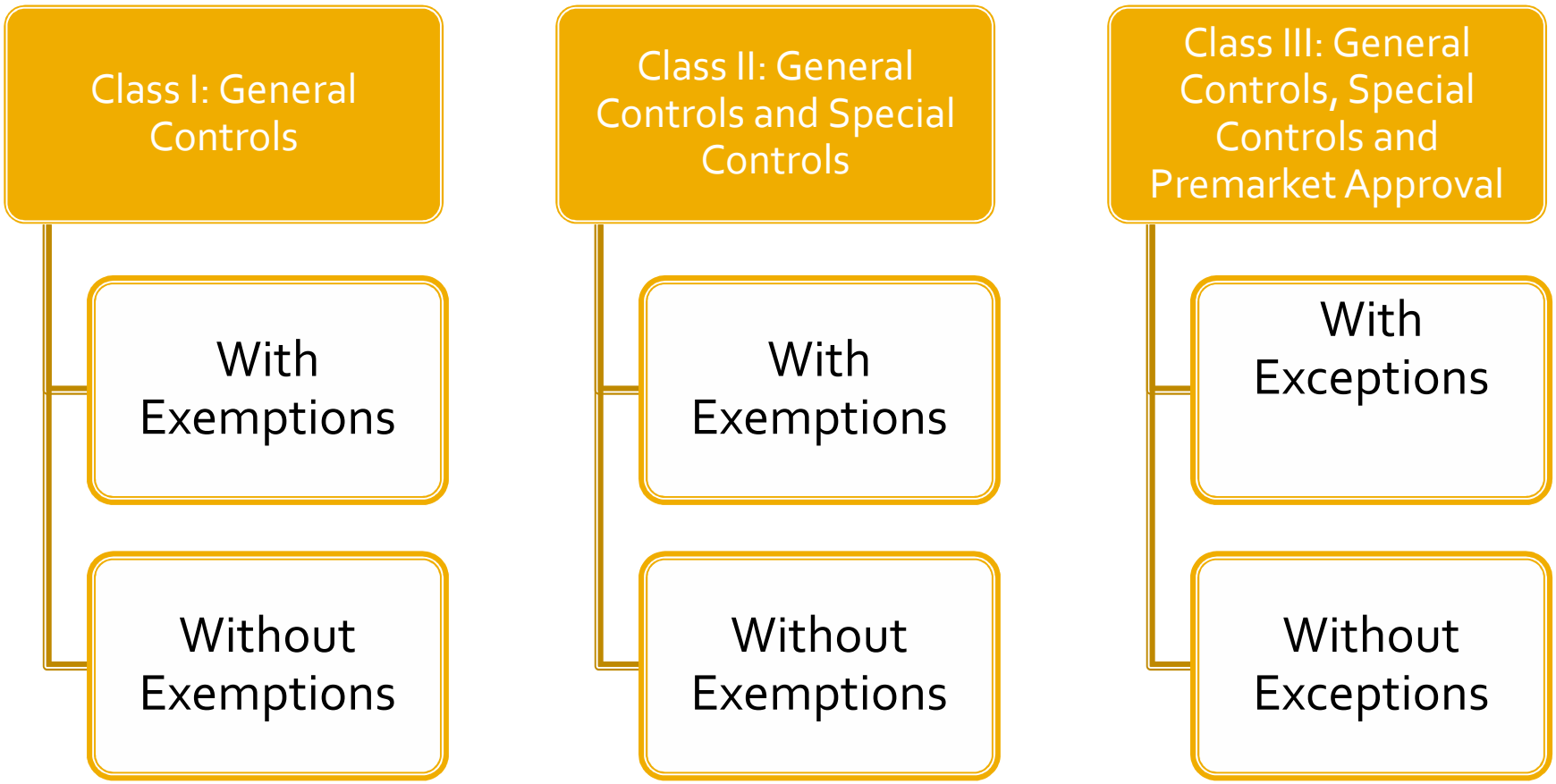
Special Controls

- Special Labeling requirements
- Recommendation to follow FDA certain guidances
- Mandatory performance standards
- Human clinical trials
- Postmarket surveillance requirements

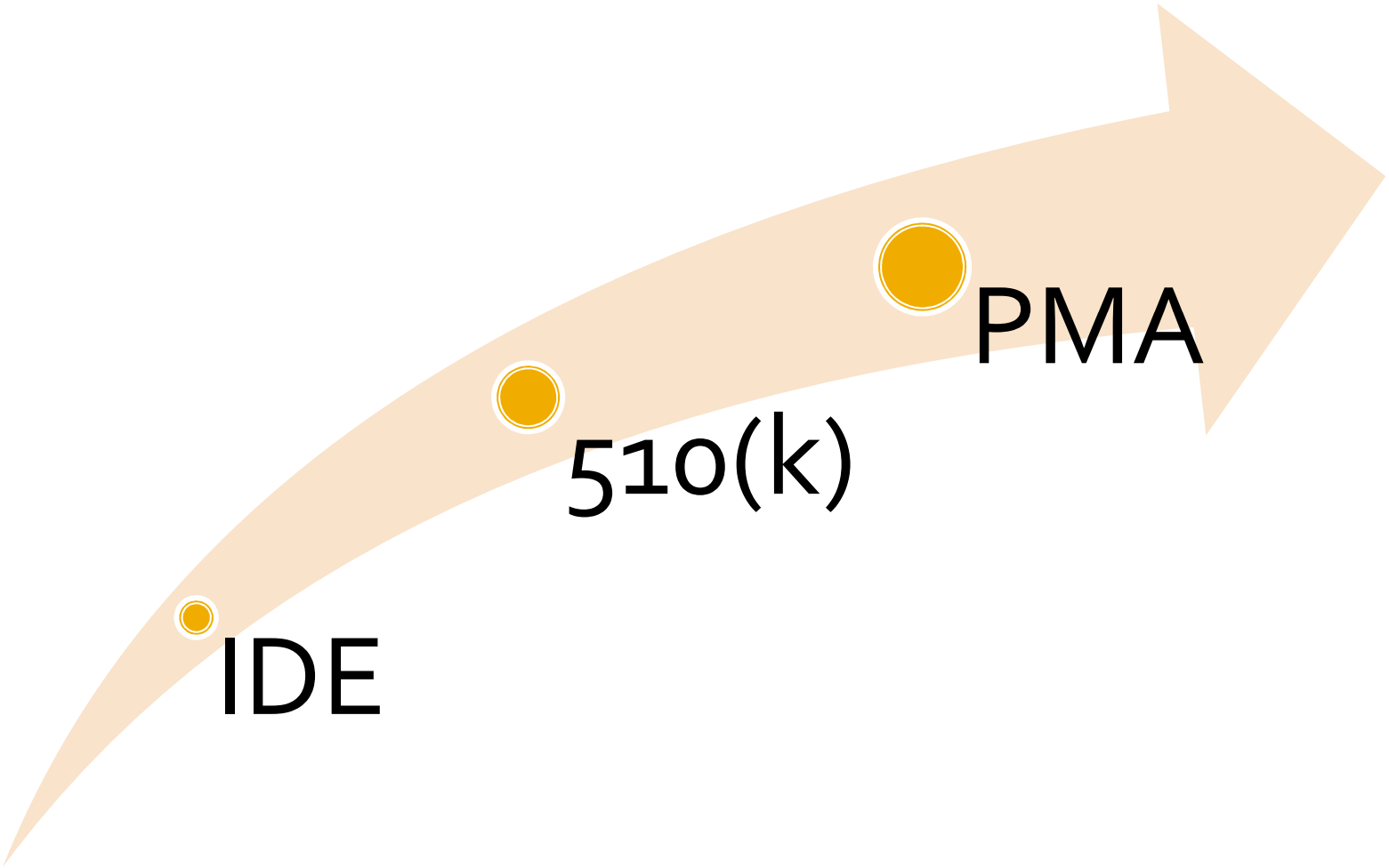
Premarket Approval

- Stringent scientific and regulatory review and approval

Device Class and Controls

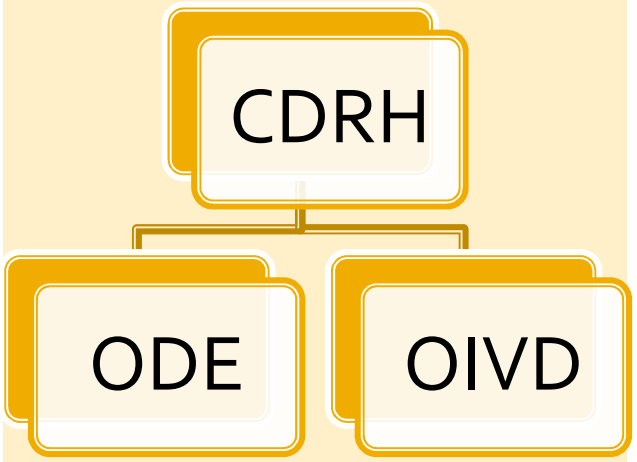


Device Review Mechanism



Review Offices and Device Panels

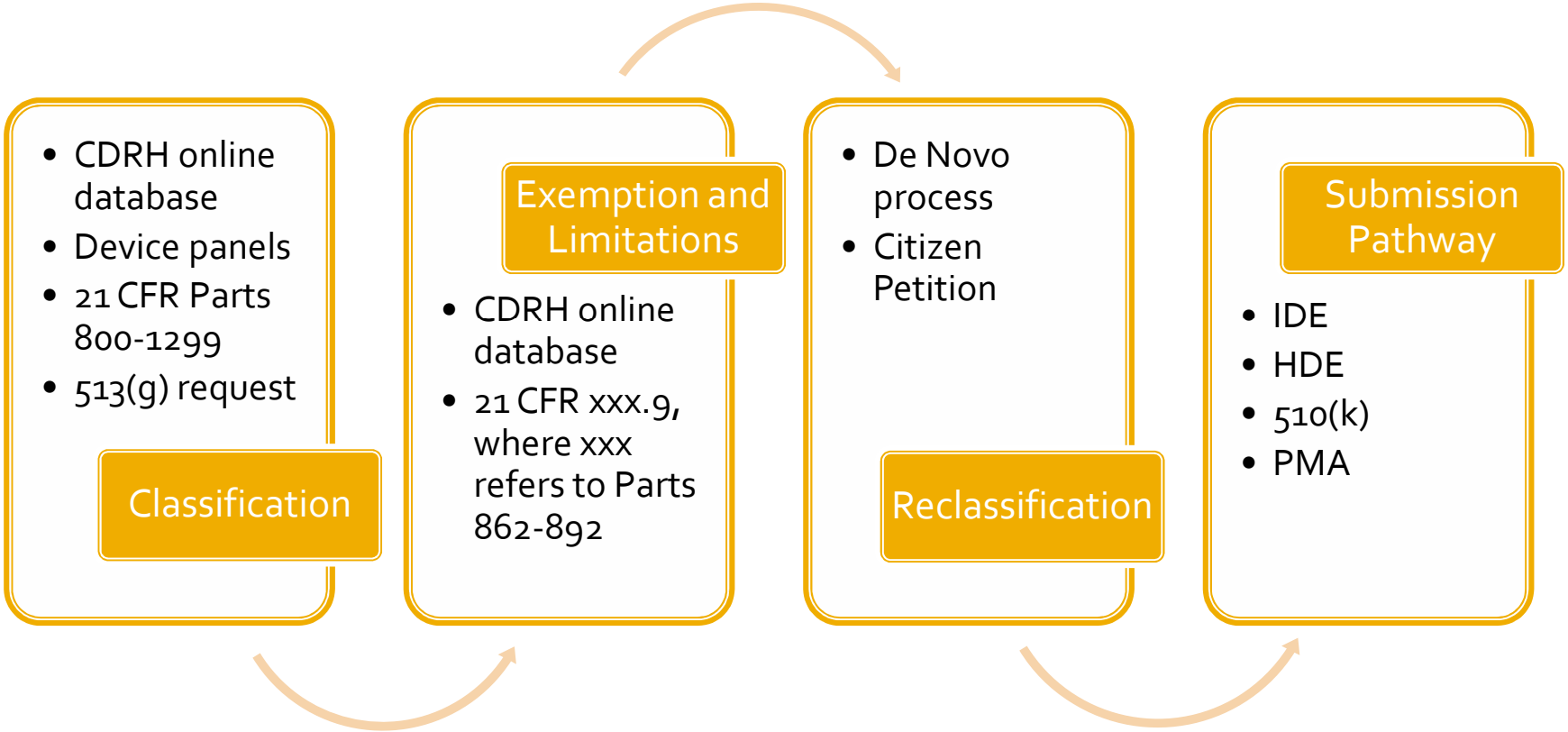
2 REVIEW OFFICES



16 MEDICAL SPECIALTY PANELS

1. Anesthesiology
2. Cardiovascular
3. Clinical Chemistry and Clinical Toxicology
4. Dental
5. Ear, Nose, and Throat
6. Gastroenterology and Urology
7. General and Plastic Surgery
8. General Hospital and Personal Use
9. Hematology and Pathology
10. Immunology and Microbiology
11. Neurology
12. Obstetrical and Gynecological
13. Ophthalmic
14. Orthopedic
15. Physical Medicine
16. Radiology

General Process for Device Submission



IDE Process

Review and Approval:

- Nonsignificant risk device: Abbreviated IDE (21 CFR 812.2(b))
- Significant risk device: Full IDE (21 CFR 812.20)

Review Time:

- 30 days

Review Fees

- IRB: review fee varies
- FDA: no fee

Full IDE Application Contents

1. Sponsor information
2. Investigational plan
3. Report of prior investigations
4. MFC (methods, facility, & controls)
5. Investigator agreement form
6. Investigators information
7. IRB chairperson information
8. Certification
9. Informed consent related materials

510(k) Process

1	2	3	4
Product code	**Predicate device**	**Substantial equivalence**	**Submission Method**
• CDRH online database • 513(g)	• CDRH online database	• Technology • Safety and effectiveness	• Traditional • Abbreviated • Special

Device Subject to 510(k)*

- A non-exempted Class I device
- A non-exempted Class II device
- A Class III device for which PMA is not required**
- A device exceed the limitations of exemptions specified in (21 *CFR* 862.9 or 21 *CFR* 864.9) ***

When a 510(k) submission is required?

1. New class I or Class II device, unless exempted by regulation (check FDA website for list of exempted devices)
2. Certain Class III devices on the market prior to 1 December 1990
3. Modification of legally marketed devices that could be expected to have a significant effect on the safety or effectiveness of the device
4. Significantly change the intended use or add a new intended use

Who is Required to Submit a 510(k)

- Domestic manufacturers introducing a device to the U.S. market
- Specification developers introducing a device to the U.S. market
- Repackers or relabelers who make labeling changes or whose operations significantly affect the device
- Foreign manufacturers/exporters or U.S. representatives of foreign manufacturers/exporters introducing a device to the U.S. market

Exemption

- Most of Class I and some Class II devices are exempted from 510(k)
- New device that is substantially equivalence to preamendment Class III device that are not required for PMA is exempted from PMA but is required with 510(k)
- Class I devices exempted from 510(k) is also exempted from QSR except for general records and complaint files.
- Many 510(k) exempted Class II devices are not exempted from QSR.

Exemptions from 510(k)

- A custom device
- A device that is not generally available in finished form
- A device not offered through labeling or advertising for commercial distribution
- A device is intended for use by a patient named in the physician's or dentist's order or is intended for use by a physician or dentist and is not generally available to other physicians or dentists
- Distributors of a pre-amendment device
- Distributors of legally marketed device submitted by another person

Predicate Device

- Predicate device: any legally U.S. marketed device*
  1. a device that was legally marketed prior to May 28, 1976 (a preamendments device)
  2. a device that has been cleared through the 510(k) process
  3. a device that was originally on the U.S. market as a Class III device (Premarket Approval) and later downclassified to Class II or I
  4. a 510(k) exempt device

How to Search for a Predicate Device

- 510(k) Search Engine :
- Information which can be useful to find a predicate device includes:
  1. names of similar devices - traded name under which the device is marketed;
  2. manufacturer(s) of the similar device(s);
  3. marketing status, i.e., preamendments or postamendments device;
  4. 510(k) numbers for postamendments devices;
  5. classification information, i.e., product codes, classifying regulations, etc., for your device.

510(k) for class III device

- All new Class III devices required PMA instead of 510(k) except for the case
  - The similar Class III device exist before 1976 (pre amendment) for which PMA has not been called and you can find substantial equivalence to pre amendment Class III devices.
  - In the case using 510(k) for a Class III device, it must include summary and certification.

Substantial Equivalence

- The same intended use and technological characteristics as the predicate device, or if the new 510(k)device is technologically different,
- It is just as save and effective as the predicate device

(Source: 513(i)(1) of the *FD&C Act*)

510(k) Submission Methods

Traditional	Abbreviated	Special
• The original complete submission as provided in 21 CFR 807	• Modification of legally marketed device is compliant with application FDA guidances, special controls and consensus standards. • Relies on the use of guidance documents, special controls, and recognized standards to facilitate 510(k) review	• Modification of legally marketed device is compliant with Design Control

510(k) Review Time and Fees

TIME FRAMES

- Traditional: 90 days
- Abbreviated: it depends
- Special: 30 days

REVIEW FEES (FY 2009)

- 510(k): $3,693
- 513(g): $2,710
- SB 50% discount

FDA Action

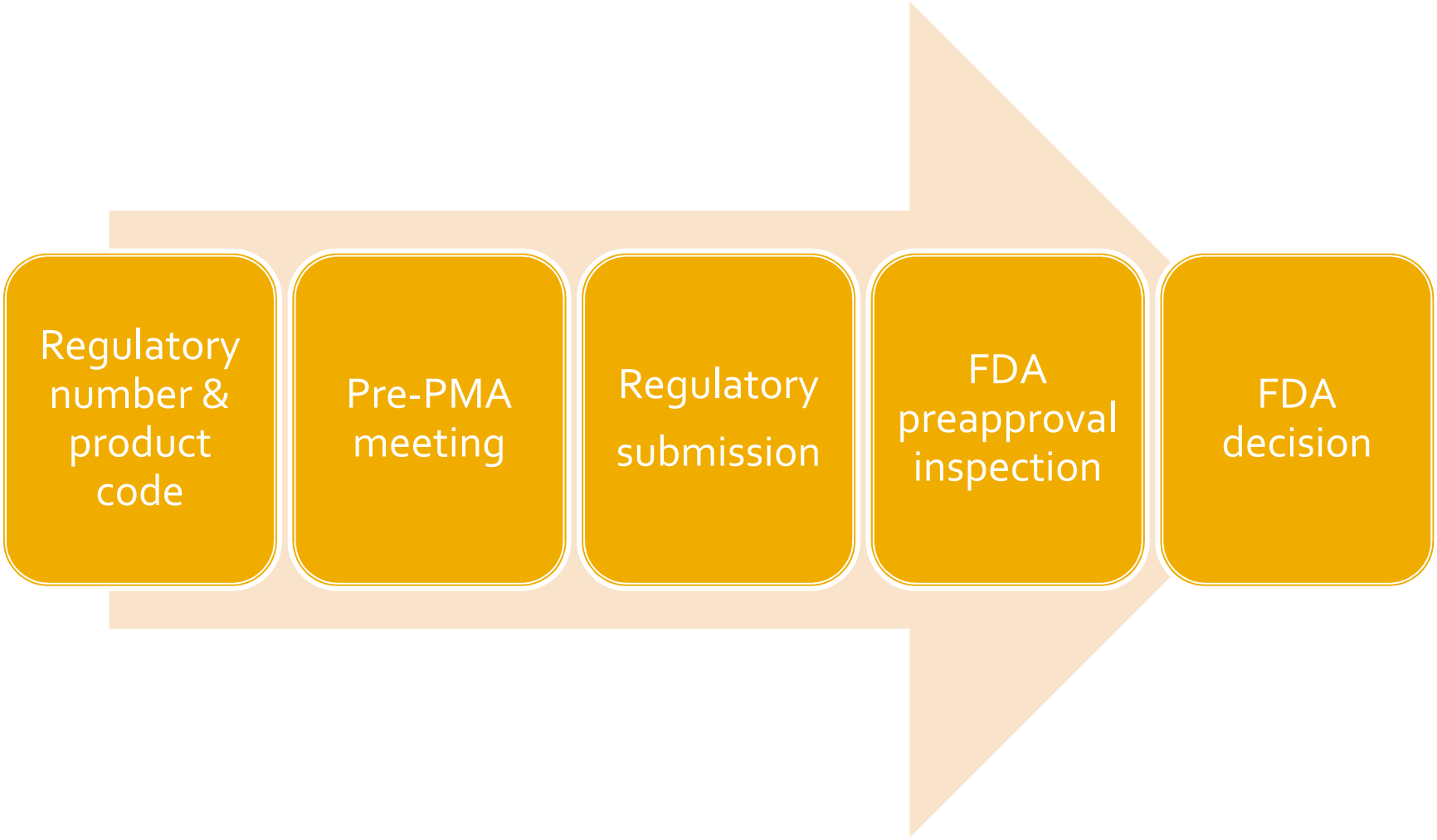
GOOD SIGN

- SE Letter (substantially equivalent)
- Request for additional information
- Advise submitter that 510(k) is not required (not a device or otherwise exempt)

BAD SIGN

- Refuse-to-Accept Letter
- NSE Letter (not substantially equivalent)

PMA Process



PMA Content and Format

- Administrative information
  - Including sponsor
  - GLP and GCP statements
- MFC information (method, facility, controls)
- Device data
- Nonclinical laboratory data
- Clinical data
- Format: http://www.fda.gov/CDRH/devadvice/pma/app_methods.html

Valid Foreign Clinical Data

- 21 CFR 860.7(c)(2)
- Declaration of Helsinki
- Applicable to the US population
- Competency of investigators
- Validation of data

PMA Review Time and Fees

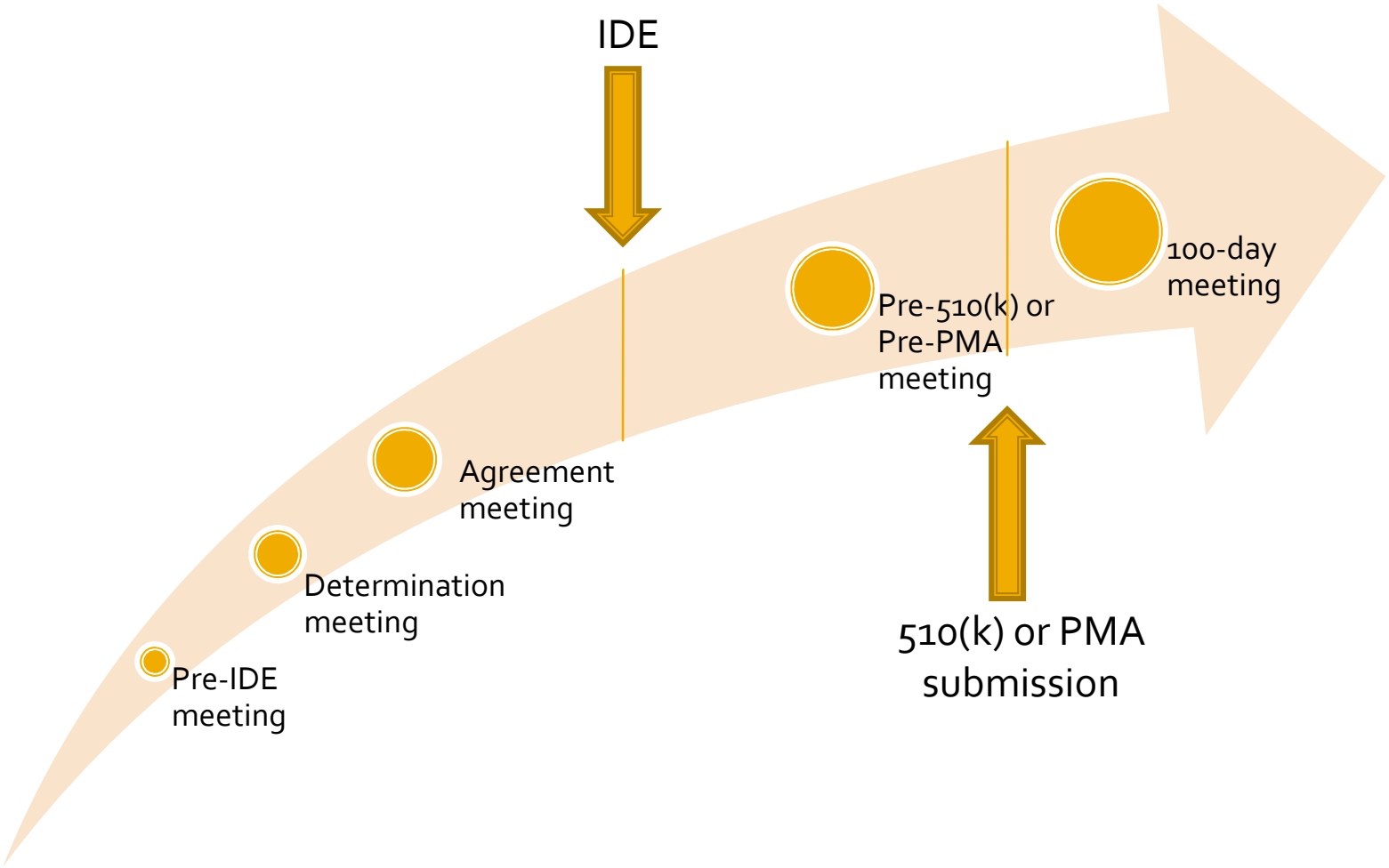
Time Frames	Fee required	Fee not required
▪ Original PMAs ▪ Filing decision: 45 days ▪ Approval decision: 180 days ▪ Total: 225 days	▪ Original PMAs ▪ Premarket reports (PMRs) ▪ Product development protocols (PDPs) ▪ Panel-track supplements ▪ 180-day supplements ▪ Real-time supplements	▪ 30-day notices ▪ 135-day supplements ▪ Special PMA Supplements-Changes Being Affected ▪ Express PMA supplements ▪ PMA annual reports

FY 2009 Device Review User Fees (U.S. Dollars)

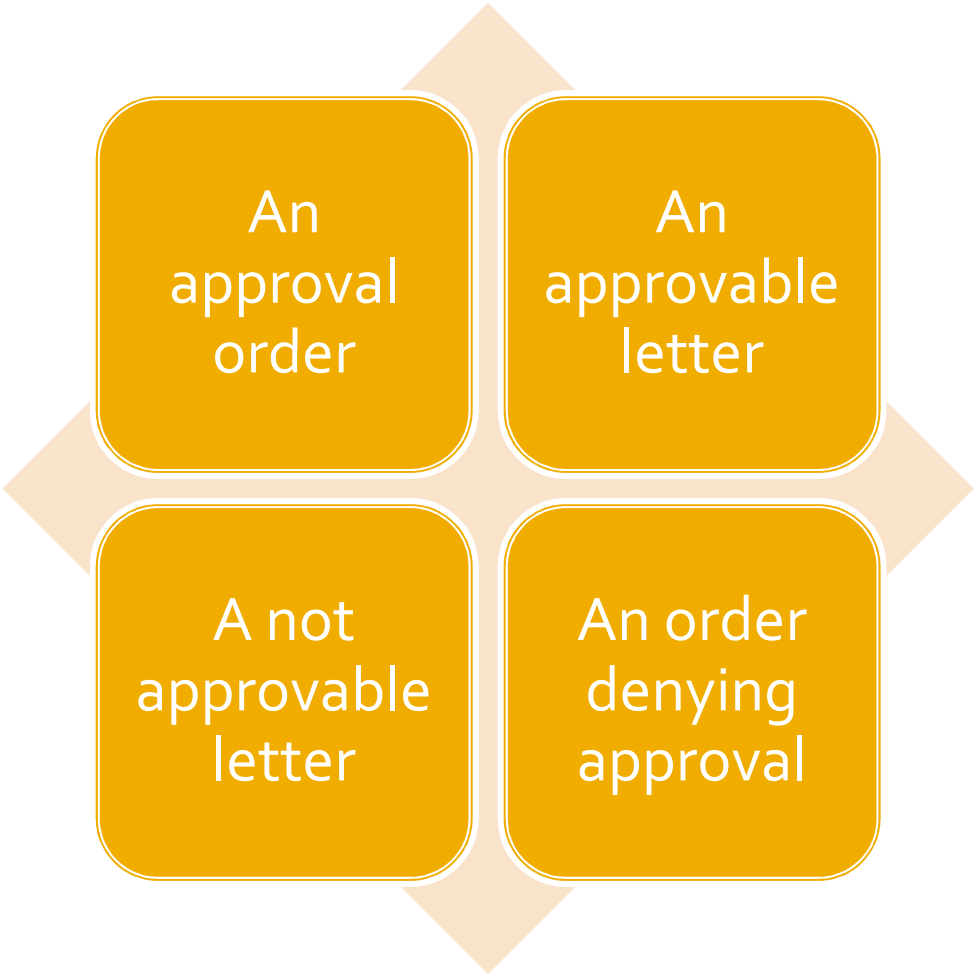
Application	Standard Fee	Small Business
Premarket Application (PMA, PDP, BLA, PMR)*	$200,725	$50,181
First premarket application from firms with gross receipts or sales ≤ $30 million	Not Applicable	Fee is Waived
Panel-track Supplement	$150,544	$37,636
Efficacy Supplement (for BLA)	$200,725	$50,181
180-day Supplement	$30,109	$7,527
Real-time Supplement	$14,051	$3,513
30-day Notice	$3,212	$1,606
FY 2009 Annual Fee for Periodic Reporting on a Class III Device (U.S. Dollars)		
	Standard Fee	**Small Business**
Annual fee for periodic reporting on a class III device	$7,025	$1,756

* PMA=Premarket Approval; PDP=Product Development Protocol; BLA=Biologics License Application; PMR=Premarket Report (for a reprocessed device)

Meeting with FDA



FDA PMA Decision



Other PMA Submission Subjects

- Panel-track PMA supplement
- 30-day PMA supplement (30-day notice)
- 180-day PMA supplement
- Real-time PMA supplement
- Modular PMA
- Streamlined PMA
- Product development protocol
- HDE

IVD

- IVD has its own definition
- IVD has its own review office
- IVD can use CeSub with CLIA Waver application

CLIA

- Clinical Laboratory Improvement Amendments (CLIA) of 1988
- quality standards for laboratory testing
- accreditation program for clinical laboratories
- three categories of testing:
  - waived tests
  - tests of moderate complexity
  - tests of high complexity

Electronic Submissions

Electronic Copy	CeSub	STEP
• Electronic copy of paper submission	• IVD 510(k) • Safety reports	• GHTF • Pilot program only