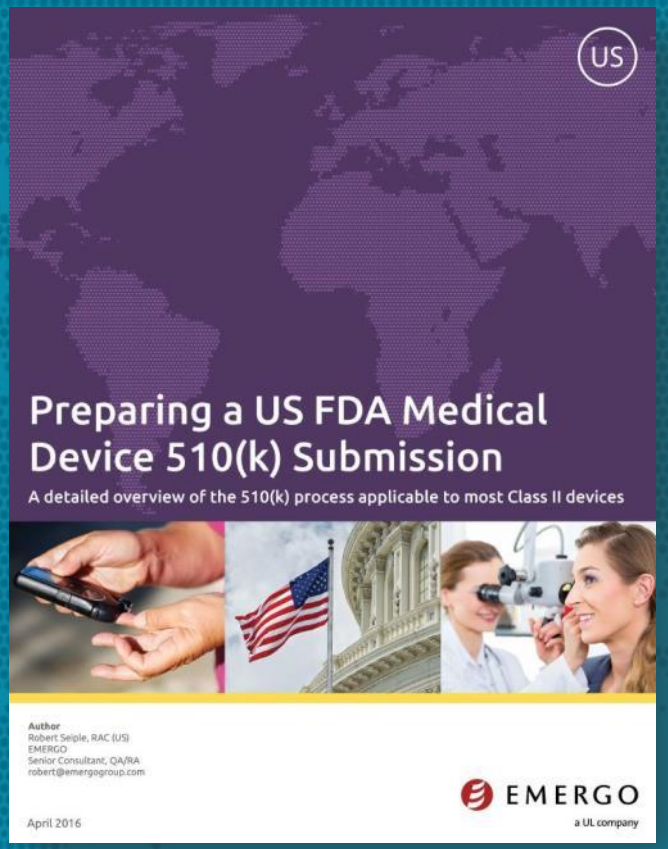
Getting US FDA clearance for your device: Improving 510(k) submissions

Audrey Swearingen, RAC
Director, Regulatory Affairs
Telephone: +1 512.222.0263
Email: aswearingen@emergogroup.com



Download this white paper
www.emergogroup.com/resources/united-states

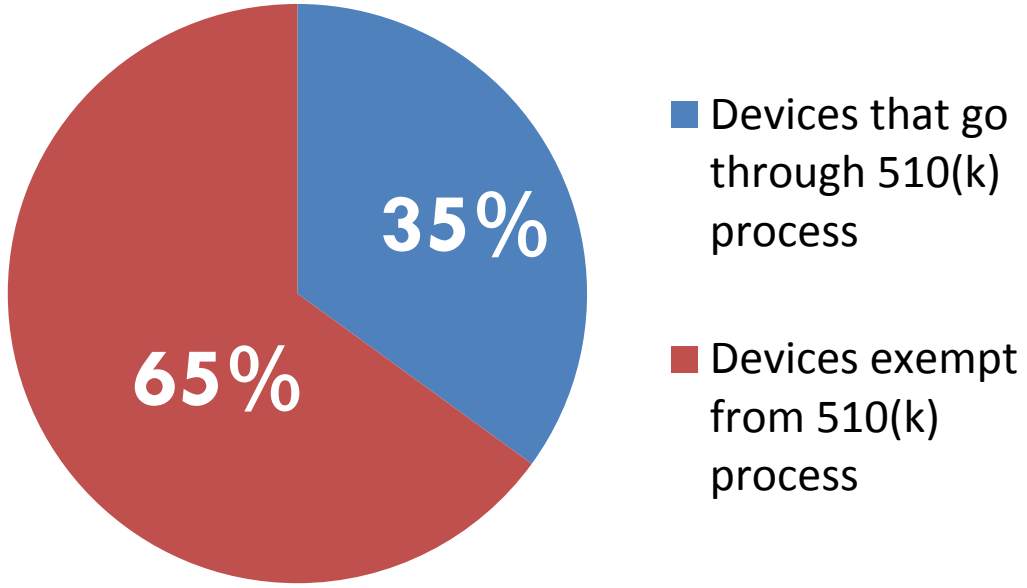
EMERGO

Agenda

- 510(k) program overview
- Role of product codes
- Role of guidance documents & standards
- Structure and content of 510(k)
- FDA review and decision process
- Common problem areas
- How to improve success

510(k) program overview - basics

- Established via 1976 Medical Devices Amendment
- Traditional (most common), Special, Abbreviated
- User fee FY2017 = US$4,690 until October 1
- ‘Substantial equivalence’ to a legally cleared device (predicate)
  - Same intended use (same FDA product code)
  - Same or similar technological characteristics



What is a predicate device?

- ✓Predicate device = Legally marketed device cleared by the FDA, or a Pre-Amendment Device
- ✓Has the same Intended Use – General purpose or function
- ✓Indications for Use may be slightly different (but as close as possible)

What is a predicate device?

- ✓Has same or similar technological characteristics to your device
- ✓Single Primary Predicate must be identified
- ✓Secondary predicate(s) acceptable in some cases
- ✓Recently cleared device; still on the market
- ✓No device-related recalls

What is substantial equivalence?

FD&C Act, section 513(i):

The term "substantially equivalent"….means, with respect to a device being compared to a predicate device, that the device has the same intended use as the predicate device and…

(i) has the same technological characteristics as the predicate device, or

(ii)(I) has different technological characteristics and the information submitted…. including appropriate clinical or scientific data if deemed necessary…. demonstrates that the device is as safe and effective as a legally marketed device, and (II) does not raise different questions of safety and effectiveness than the predicate device.

Different technological characteristics

The term “different technological characteristics” means, with respect to a device being compared to a predicate device, that there is a significant change in the materials, design, energy source, or other features of the device from those of the predicate device.

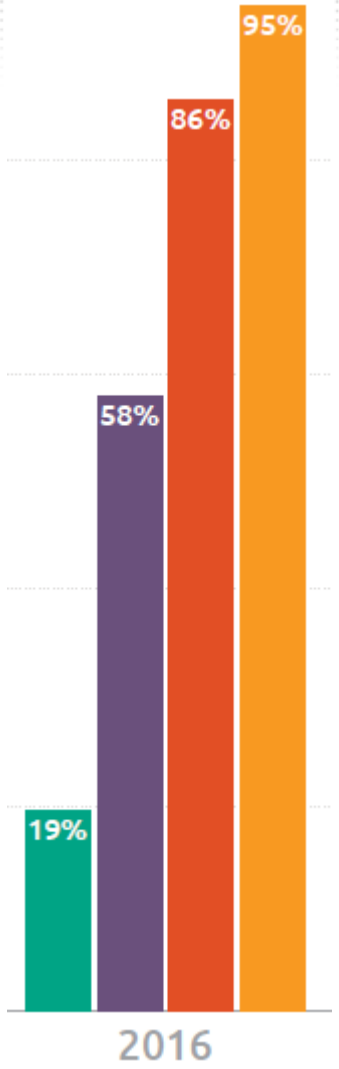
Must justify the differences - cannot simply state ‘no difference to safety and effectiveness.’

Evaluating Substantial Equivalence guidance document

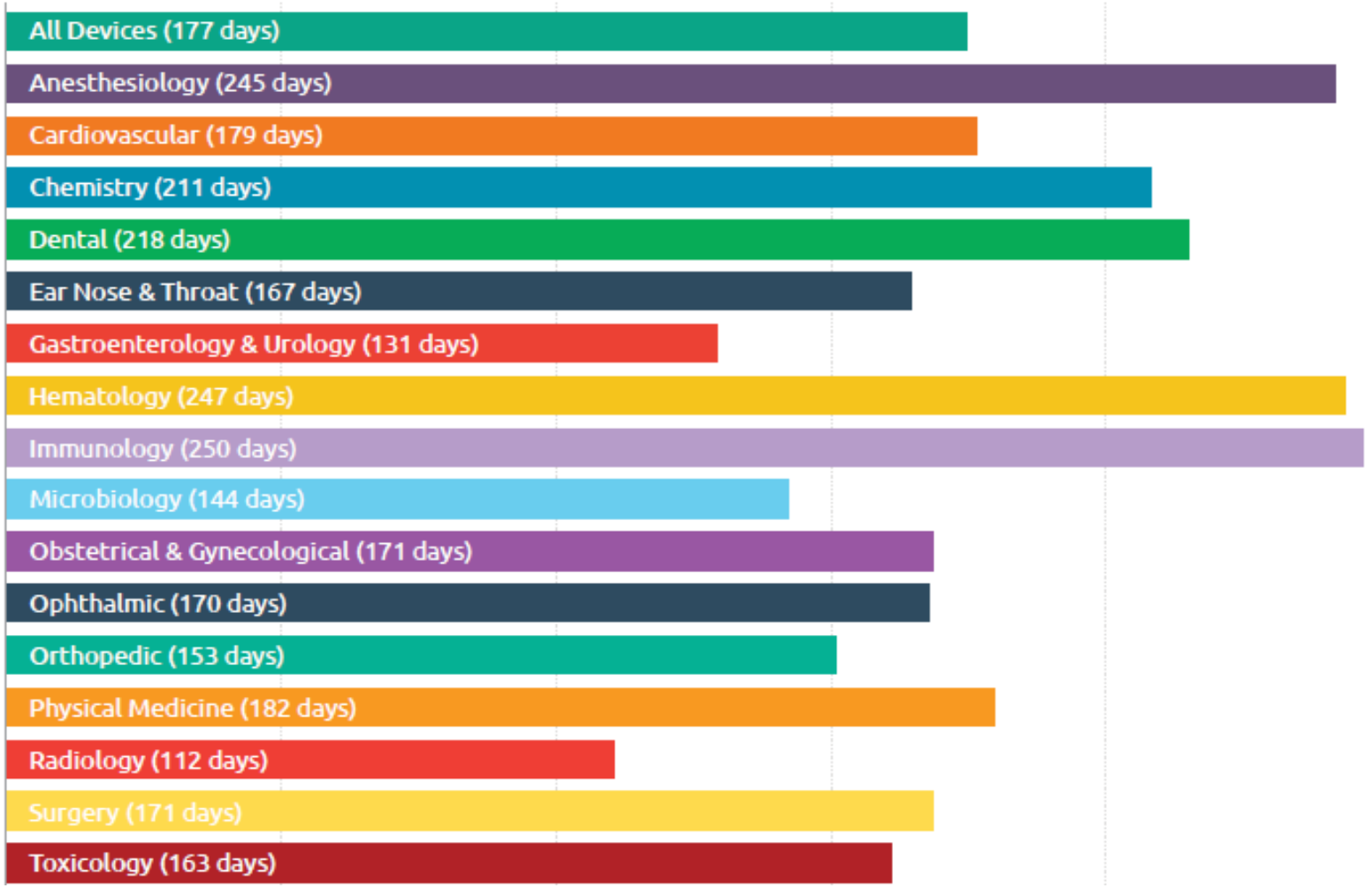
510(k) program overview – stats from 2016

- Traditional 510(k) average time to clearance = **177 days**
- Special 510(k) average time to clearance = **67 days**
- Number of 510(k) applications cleared in 2016 = **2,957**
- Percent of 510(k)s cleared:
  - **Within 3 months**: 19%
  - **Within 6 months**: 58%
  - **With 9 months**: 86%
  - **Within 12 months**: 95%

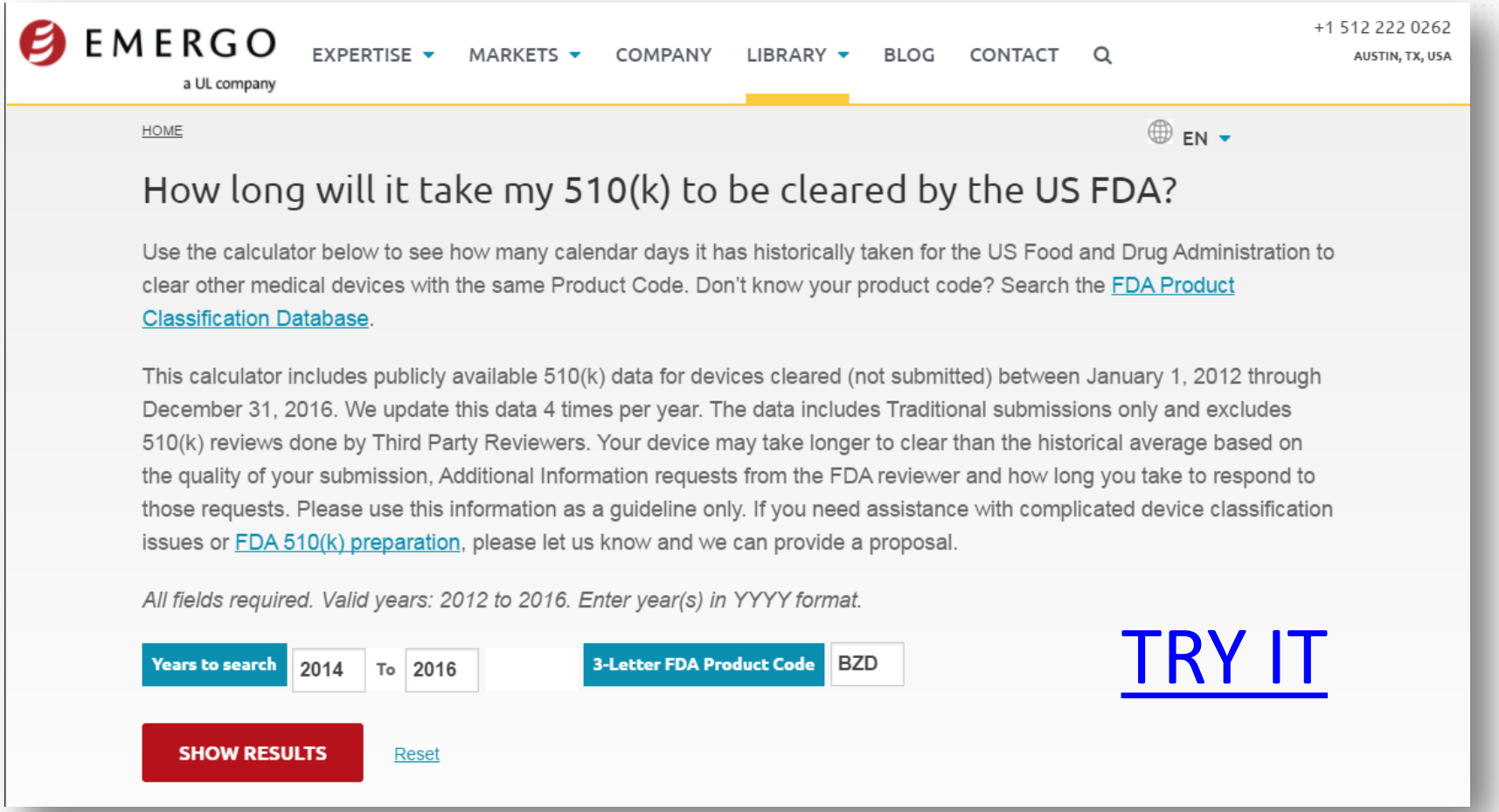
(Source)



Average calendar days from submission to clearance



How long will your device take to clear?



https://www.emergogroup.com/resources/united-states/fda-510k-calculator

Use of Product Codes

What is a product code?

- A 3-letter combination FDA has assigned to a specific device type
- Defines and describes the device
- Corresponds to device classification and submission requirements
- Multiple product codes fall under a single 21 CFR Reg. Number
- FDA product classification database - link

1 to 4 of 4 Results
886.5916

Results per Page 5

New Search

Export to Excel Help

Product Code	Device		Regulation Number	Device Class
MUW	Lens, Contact (Orthokeratology)	Rigid Gas Permeable Contact Lens	886.5916	2
HQD	Lens, Contact (Other Material) - Daily	Rigid Gas Permeable Contact Lens	886.5916	2
NUU	Lens, Contact, Orthokeratology, Overnight	Rigid Gas Permeable Contact Lens	886.5916	3
MWL	Lens,Contact(Rigid Gas Permeable)-Extended Wear	Rigid Gas Permeable Contact Lens	886.5916	3

Product Code ‘HQD’

- Class II
- 510(k) submission
- Reg # 886.5916 - *intended to be worn directly against the cornea to correct vision conditions. …made of various materials, […] whose main polymer molecules generally do not absorb or attract water.*
- 10 Consensus Standards
- No device Guidance Document
- Not exempt from GMP (QSR)

Device	Lens, Contact (Other Material) - Daily
Regulation Description	Rigid gas permeable contact lens.
Regulation Medical Specialty	Ophthalmic
Review Panel	Ophthalmic
Product Code	HQD
Premarket Review	Office of Device Evaluation (ODE) Division of Ophthalmic and Ear, Nose and Throat Devices (DOED) Contact Lenses and Retinal Devices Branch (CLRD)
Submission Type	510(k)
Regulation Number	886.5916
Device Class	2
Total Product Life Cycle (TPLC)	TPLC Product Code Report
GMP Exempt?	No

Recognized Consensus Standards

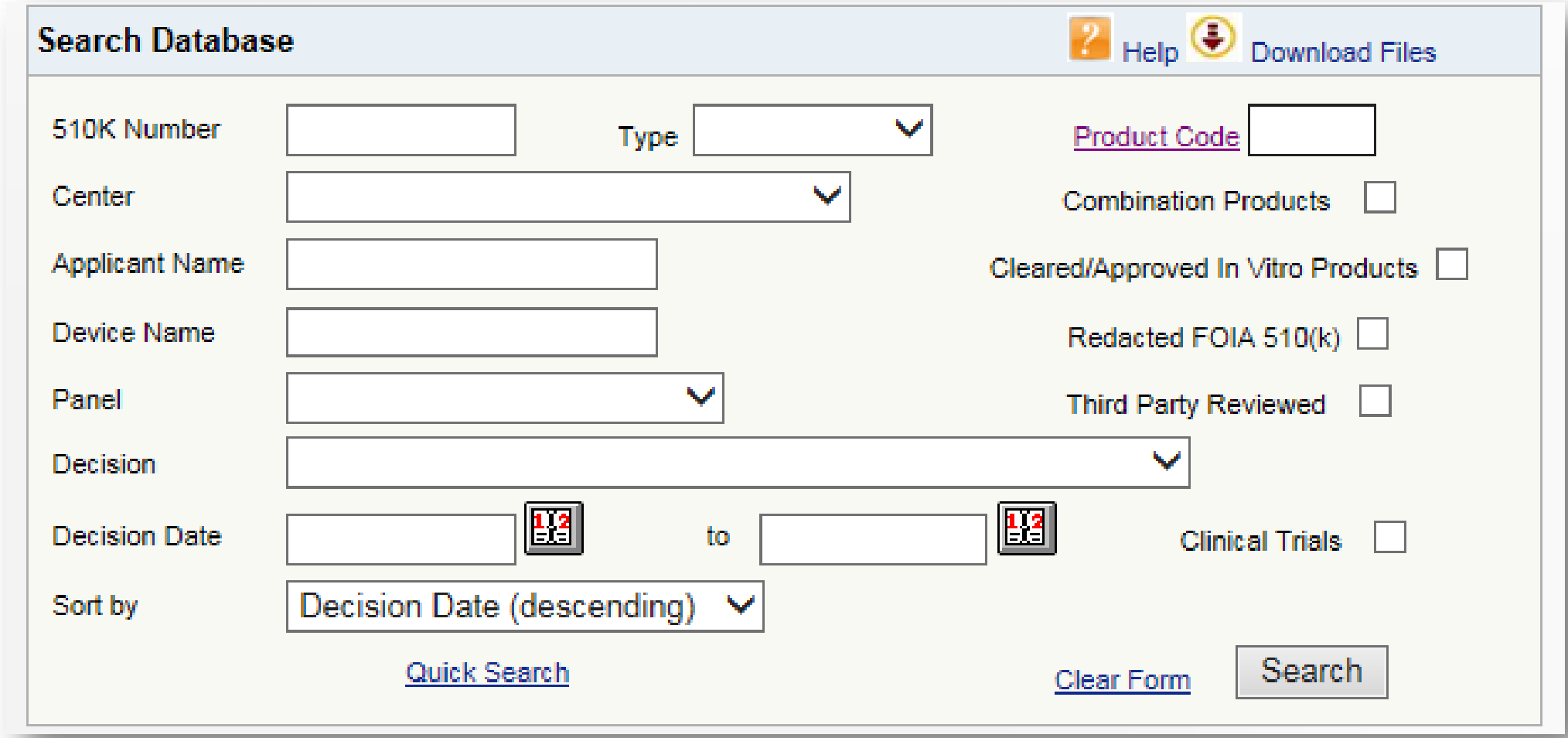
- 10-46 ISO 18369-3 First edition 2006-08-15
  Ophthalmic optics - Contact lenses - Part 3: Measurement Methods
- 10-54 ISO 18369-4 First edition 2006-08-15
  Ophthalmic optics - Contact lenses - Part 4: Physicochemical properties of contact lens materials
- 10-60 ISO 11981 Second edition 2009-07-01
  Ophthalmic optics -- Contact lenses and contact lens care products -- Determination of physical compatibility of contact lens care products with contact lenses
- 10-67 ISO 11986 Second edition 2010-11-01
  Ophthalmic optics -- Contact lenses and contact lens care products -- Guidelines for determination of preservation uptake and release
- 10-77 ISO 9394 Third edition 2012-10-01
  Ophthalmic optics -- Contact lenses and contact lens care products -- Determination of biocompatibility by ocular study with rabbit eyes
- 10-83 ISO 18369-1 First edition 2006-08-15
  Ophthalmic optics -- Contact lenses -- Part 1: Vocabulary, classification system and recommendations for labeling specifications [Including: Amendment 1 (2009)]
- 10-85 ISO 11980 Third edition 2012-11-15
  Ophthalmic optics -- Contact lenses and contact lens care products -- Guidance for clinical investigations
- 10-88 ASTM D790-10
  Standard Test Methods for Flexure Properties of Unreinforced Plastics and Electrical Insulating Materials
- 10-100 ISO 18259 First Edition 2014-10-01
  Ophthalmic optics - Contact lens care products - Method to assess contact lens care products with contact lenses in a lens case, challenged with bacterial and fungal organisms
- 10-101 ISO 18189 First edition 2016-06-01
  Ophthalmic optics - Contact lenses and contact lens care products - Cytotoxicity testing of contact lenses in combination with lens care solution to evaluate lens/solution interactions

Implanted Device?	No
Life-Sustain/Support Device?	No

How are product codes used in 510(k) process?

1. Determine Classification of Device
   - ✓Search Classification database for appropriate Product Code
2. Identify Submission Type
   - ✓Product classification page states if device requires a 510(k), PMA, or is exempt
3. Identify applicable Recognized Consensus Standards / Guidance
4. Find Predicate Devices
   - ✓Search 510(k) Database using the identified Product Code
   - ✓Review Device Names for applicability
   - ✓Review 510(k) Summary of potential predicates

Search 510(k) database for predicate using product code



Cleared 510(k) devices under product code HQD

1 to 25 of 94 Results
ProductCode: *hqd* **Decision Date To:**
07/10/2017

1 2 3 4 >

Results per Page 25

New Search

Export to Excel | Download Files | More About 510(k)

Device Name	Applicant	510(K) Number	Decision Date
Acuity 85 (Oprifocon A) Rigid Gas Permea	Acuity Polymers, Inc.	K170001	06/02/2017
Acuity 58 (Enflufocon B) Rigid Gas Perme	Acuity Polymers, Inc.	K170007	05/31/2017
Custom Stable(Tm) Rigid Gas Permeable Sc	Valley Contax, Inc.	K170335	03/24/2017
Acuity 18 (Enflufocon A) Rigid Gas Perme	Acuity Polymers, Inc.	K163254	01/18/2017
Acuity 100 (Hexafocon A) Rigid Gas Perme	Acuity Polymers, Inc.	K162005	12/08/2016
Synergeyes A&M (Paflufocon D Hem-Iberfil	Synergeyes, Inc.	K153714	11/15/2016
Hidrocor, Hidrocharme, And Natural Color	Solotica	K160472	08/10/2016
Optimum Gp With Hpt (Roflufocon A, B, C,	Contamac Ltd.	K161100	08/10/2016
Synergeyes Sih With Hydra-Peg(Petrafocon	Synergeyes, Inc.	K160938	08/01/2016
Bostonsight Pd Prosthetic Device	Bostonsight	K161461	07/25/2016

Predicate evaluation exercise

Example:

Q: Can a Vascular Infusion set with PVC tubing be compared to an Infusion set with silicone tubing, if they have same Intended Use?

A: Yes; if data demonstrates that the PVC material does not raise new questions of safety and effectiveness as compared to the silicone.

- ✓ Biocompatibility
- ✓ Performance – Pressure, Handling, Clamping force
- ✓ Sterilization

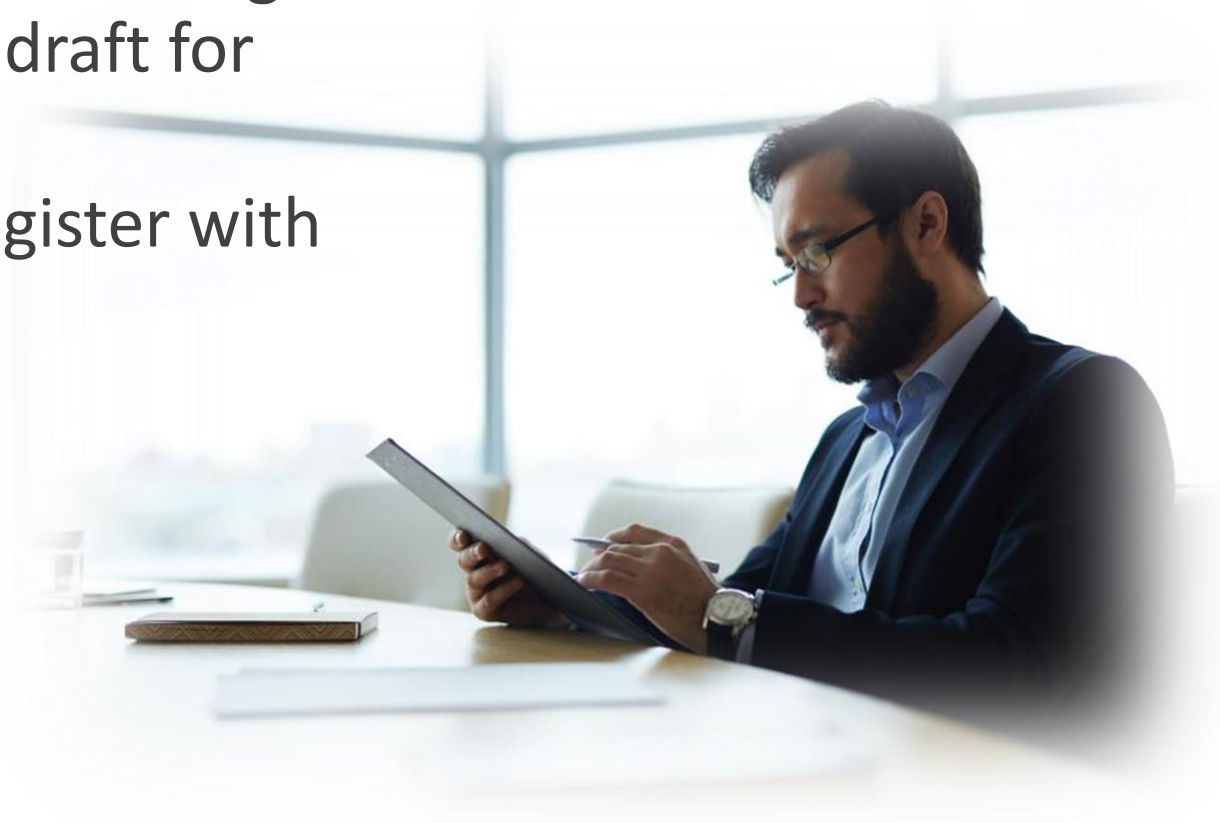
Role of Guidance Documents and Standards

FDA guidance documents

- *Not* a regulation (not legally binding), but based on the regulations
- Conveys FDA's current thinking / expectations on a particular topic:
  - Beneficial for guiding development, testing, labeling, 510(k) preparation, etc.
  - Strongly advisable to read, understand and utilize!
  - If you do not follow a guidance document, must justify why your approach meets the regulatory requirements.

FDA guidance documents and where to find them

- Undergoes a Public Comment period during draft phase – FDA posts release of draft for comment
- Final is published in the Federal Register with public's comments / FDA response
- Types of guidance documents:
  - General Topic (e.g., Patient Labeling; Biocompatibility Testing)
  - Device Specific (Special Controls)
- Guidance website



Required testing for 510(k) - Standards

Manufacturer is responsible for ensuring device is safe and effective.

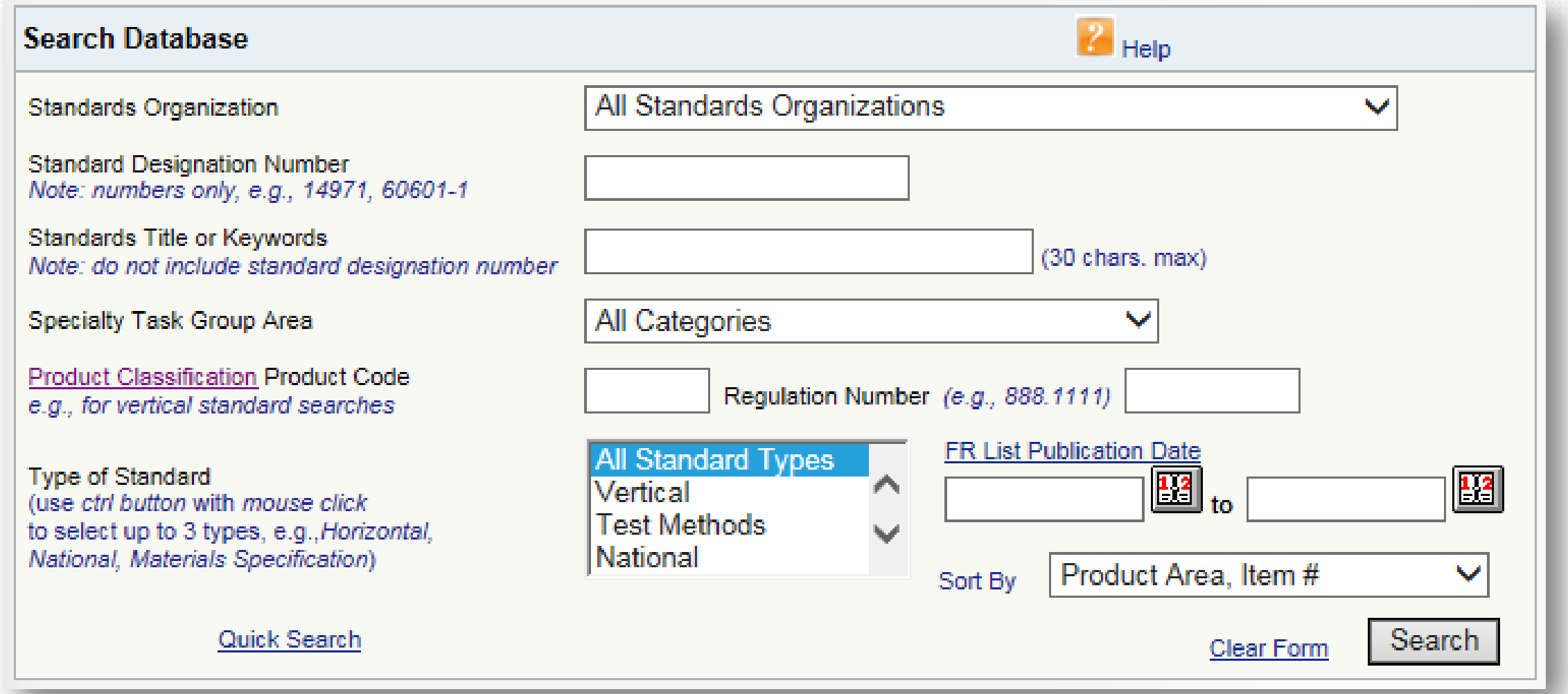
- Perform Design, Process, and Clinical Risk Assessments
- Design-related testing (mechanical, packaging, performance)
- Process-related testing (sterilization, transportation)
- Use-related testing (usability, clinical)

Most of these have standards

Recognized Consensus Standards – database of standards (versions) recognized by FDA

- Compliance provides level of assurance of acceptability
- FDA requires using some recognized standards, so justification needed if don't use

FDA Standards database - link



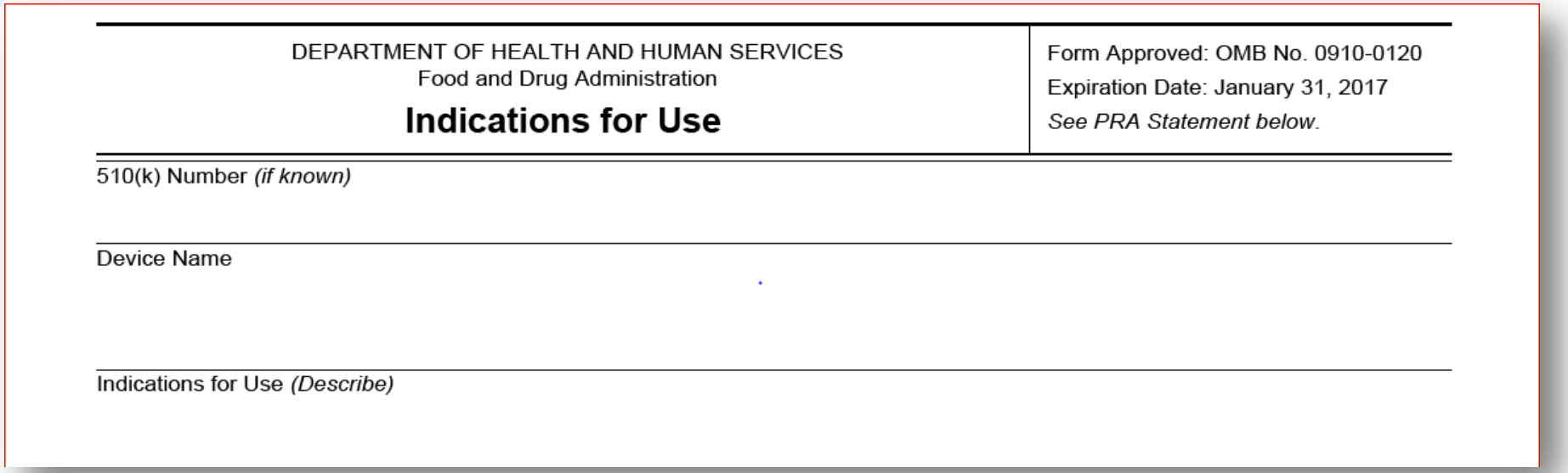
510(k) Structure and Content

510(k) guidance – follow it!

- ✓ Content and Format – link
- ✓ Content details – link
- ✓ FDA's eCopy Specification file structure – link
- ✓ Device-Specific 510(k) Requirements – Search by keyword in Guidance database – link

Required FDA forms – fill these out correctly!

1. User Fee Cover Sheet (Form 3601)
2. CDRH Premarket Review Submission Cover Sheet (Form 3514)
3. Indications for Use (Form 3881) – This must be identical to the Indications in labeling, 510(k) Summary, and other documents



DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*

Device Name

Indications for Use *(Describe)*

Required FDA forms

4. If clinical study data is included, also must have:
   - ✓ Form 3454 – Certification: Financial Interests and Arrangements of Clinical Investigators; or
   - ✓ Form 3455 - Disclosure: Financial Interests and Arrangements Of Clinical Investigators; and
   - ✓ Form 3674 – Certification of Compliance with Requirements of ClinicalTrials.gov Data Bank

5. Truthful and Accurate Statement – signed/dated by responsible person on applicant's letterhead

Required FDA forms

6. Standard Data Report Form (Form 3654) – for each standard cited

STANDARDS DATA REPORT FOR 510(k)s
(To be filled in by applicant)

This report and the Summary Report Table are to be completed by the applicant when submitting a 510(k) that references a national or international standard. A separate report is required for each standard referenced in the 510(k).

TYPE OF 510(K) SUBMISSION

☐ Traditional ☐ Special ☐ Abbreviated

STANDARD TITLE [1]

Please answer the following questions	Yes	No
Is this standard recognized by FDA [2] ?	☐	☐
FDA Recognition number [3] #		
Was a third party laboratory responsible for testing conformity of the device to this standard identified in the 510(k)?	☐	☐
Is a summary report [4] describing the extent of conformance of the standard used included in the 510(k)?	☐	☐

Section 5 – 510(k) Summary (published)

Prescribed information listed in 21 CFR 807.92

FDA guidance document - Evaluating Substantial Equivalence in 510(k)s

- ✓Administrative & regulatory information
- ✓Device description summary
- ✓Intended Use
- ✓Predicate device information
- ✓Comparison to predicate device - discussion
- ✓Non-clinical tests performed / results
- ✓Standards used
- ✓Clinical Testing Summary (if applicable)
- ✓Statement of Substantial Equivalence

Other sections / documents

- ✓ Discrete sections for each topic
- ✓ Enough detail for the FDA to completely understand what the device is and how it operates, how it is sterilized, packaged, tested, etc.
- ✓ Identify supporting attached documents (labels, reports)
- ✓ Ensure you provide controlled documents with number/rev; date; etc.
- ✓ Where possible, make a statement of comparison to the predicate device

Submitting the 510(k) and what happens next

Submitting the 510(k) to FDA

- ✓Submit 1 hard copy and an eCopy (CD, not electronic submission) – must be identical
- ✓Follow eCopy specifications – validation tool
- ✓Submit the 510(k) User Fee prior to sending 510(k) – the User Fee number is entered on Form 3514 (CDRH Submission Cover Sheet)

Submitting the 510(k)

- ✓Send to correct address; include Document Mail Center number!
- ✓If any information (graphs, color-coding) is in color, be sure to print in color
- ✓Conduct a peer review (new pair of eyes)

Refuse To Accept (RTA) Review

Refuse to Accept Policy for 510(k)s – guidance document:

- Acceptance Review based on a defined Checklist
- Assess if 510(k) is administratively complete (is anything missing?)
- Will issue an RTA letter to applicant within 15 days
- Have 180 days to provide missing information
- Review clock does not start until FDA receives response that is accepted
- If no RTA, FDA usually sends acceptance letter for substantive review

Substantive Review

- Additional Information (AI) Requests – more information needed to determine if SE
  - Stops the review clock
  - Response due within 180 days
- Not an iterative review – FDA only mandated to allow a single AI cycle
- Interactive Review – 'Real time' communications (email) – Clock does not stop!
  - Clarifications
  - Administrative revisions
  - Final remaining minor gaps
- If cannot provide requested information, should withdraw 510(k)
- If found NSE, will publish in the 510(k) database – publically accessible
- Can discuss deficiencies with FDA in a Submission Issues Meeting

Guidance- Communication During Review of Submissions guidance document

Common 510(k) problem areas[1, 2]

1. Performance testing inadequate
2. Not following guidance document
3. Inadequate device description
4. Predicate device comparison missing or lacking information
5. Problems with Indications for Use
6. Instructions for Use inadequate
7. Biocompatibility information missing or inadequate

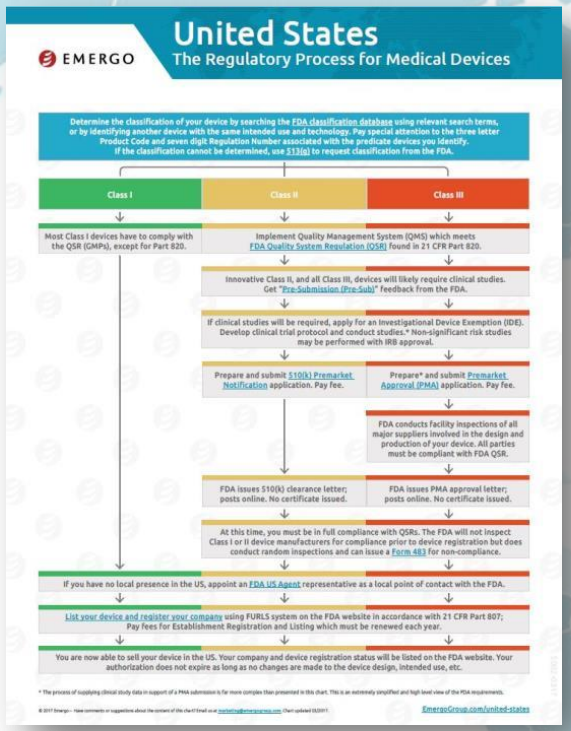
[1] Analysis Of Premarket Review Times Under The 510(k) Program

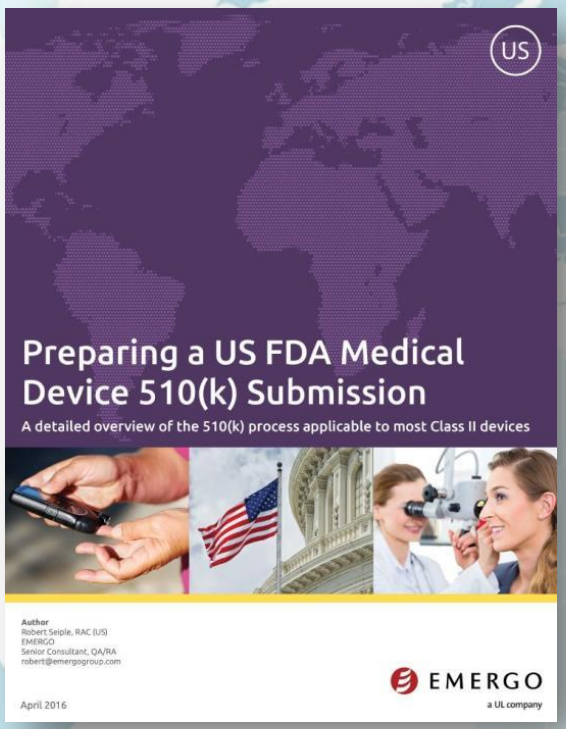
[2] Items in red are top deficiencies seen by Emergo

Final advice for 510(k) clearance

- ✓ Understand the device's data & documentation requirements:
  - Pre-Submission meetings with FDA
- ✓ Develop high-quality protocols and reports – use reputable test firms
- ✓ Choose a suitable predicate device – Provide a robust comparison
- ✓ Follow the FDA's 510(k) format, content, and eCopy specs
- ✓ Don't make the FDA assume or interpret anything – be clear and complete
- ✓ Be respectful and cooperative when asked to provide more information, but don't be afraid to ask questions, defend your data, or discuss alternative approaches

Questions about the US? Contact us.





- FDA 510(k) preparation
- FDA QSR implementation and audits
- US Agent representation
- FDA medical device classification
- FDA Q-Sub consulting

EmergoGroup.com/united-states

Available for free download at:

www.emergogroup.com/resources/united-states

For more information:
Audrey Swearingen, RAC
Director, Regulatory Affairs
Email: aswearingen@emergogroup.com

EMERGO