Welcome to today's FDA/CDRH Webinar

Thank you for your patience while additional time is provided for participants to join the call.

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Conference Number: PWXW9364565

Dental Devices Premarket Submissions

Malvina B. Eydelman, M.D., Director,
Office of Health Technology 1 (OHT1)

Michael E. Adjodha, M.ChE., Acting Assistant Director
Restorative and Surgical Devices Team

Srinivas "Nandu" Nandkumar, Ph.D., Acting Director
Division of Dental Devices

Office of Ophthalmic, Anesthesia, Respiratory, ENT and Dental Devices
(Office of Health Technology 1 (OHT1))
Office of Product Evaluation and Quality (OPEQ)
Center for Devices and Radiological Health (CDRH)

October 2, 2019

Agenda

- Center for Devices and Radiological Health Reorganization
- Review Challenges and Opportunities for Dental Device 510(k) Submissions
  - 510(k) Process Overview
  - Dental Device Types
  - Dental Device Submission Challenges
  - Recommendations
  - Resources
- Postmarket Overview
  - Medical Device Reporting (MDR)
  - Medical Device Safety Action Plan
  - Safety Signal
  - Market Withdrawals and Recalls

Objectives

During this webinar, the FDA will:

- Clarify the premarket submissions process, including what to submit and who to work with in the Center for Devices and Radiological Health's Office of Product Evaluation and Quality (OPEQ)
- Explain information to include in a 510(k) submission in order to avoid refuse-to-accept (RTA) designation
- Clarify medical device reporting (MDR) requirements, including how to report and who should report (manufacturer, dentist, etc.)
- Discuss and answer questions from webinar participants about the premarket submissions for dental devices

Center for Devices and Radiological Health (CDRH): Reorganization

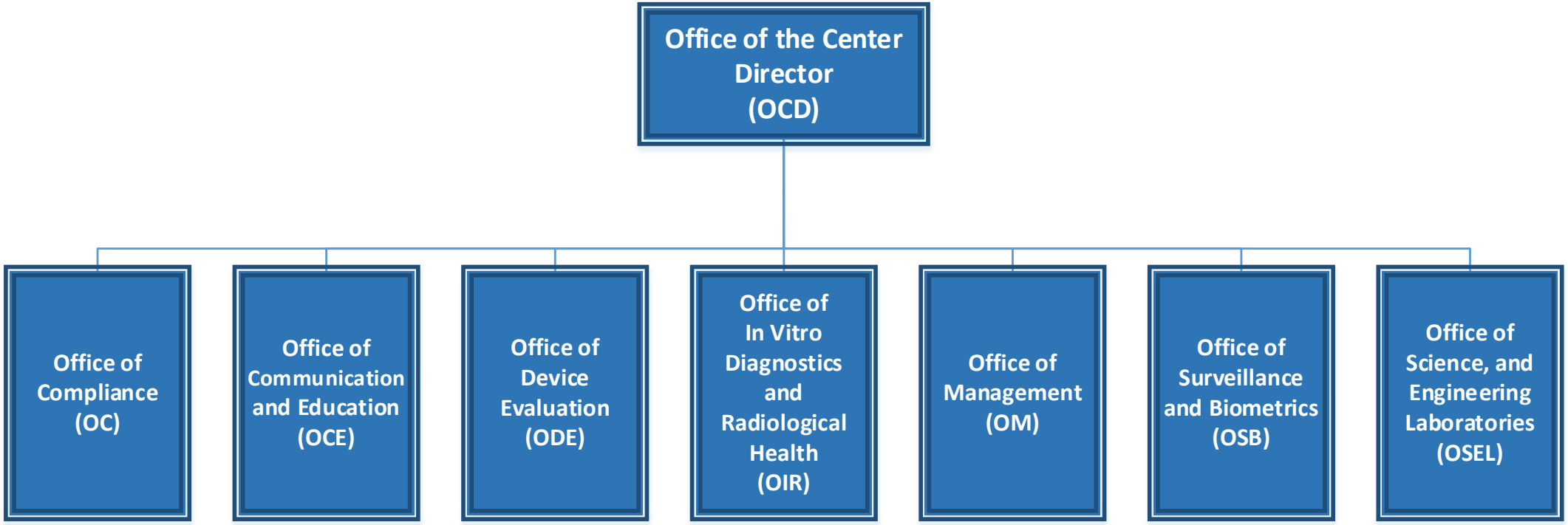
Malvina B. Eydelman, M.D.

Director
Office of Ophthalmic, Anesthesia, Respiratory, ENT and Dental Devices
CDRH, FDA

Center for Devices and Radiological Health Reorganization

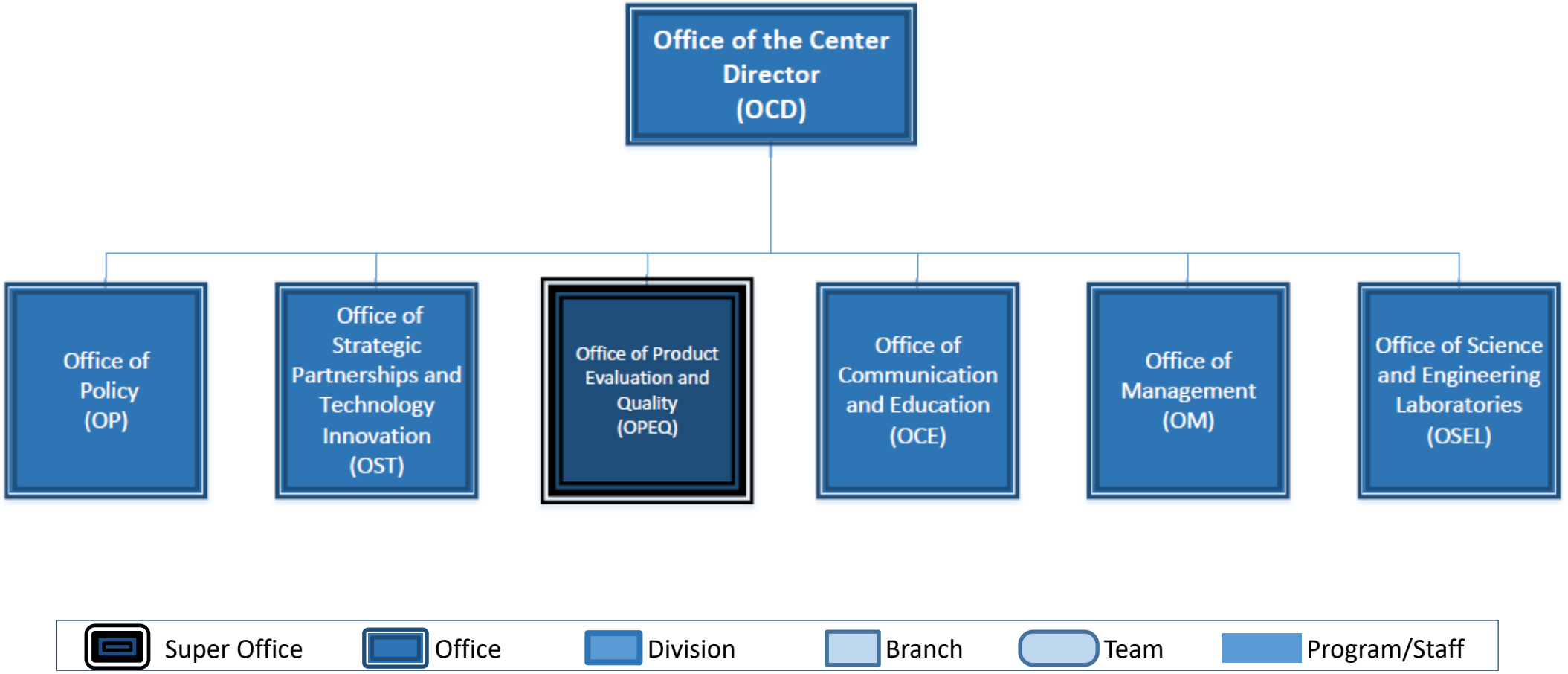
- CDRH conducted phased implementation of a Center reorganization.
- CDRH reorganization includes adopting a Total Product Lifecycle (TPLC) model and other efforts to streamline and improve efficiency and to support employees' professional growth.
- Implementation timeline: March 2019 - October 2019

CDRH Structure prior to Reorganization

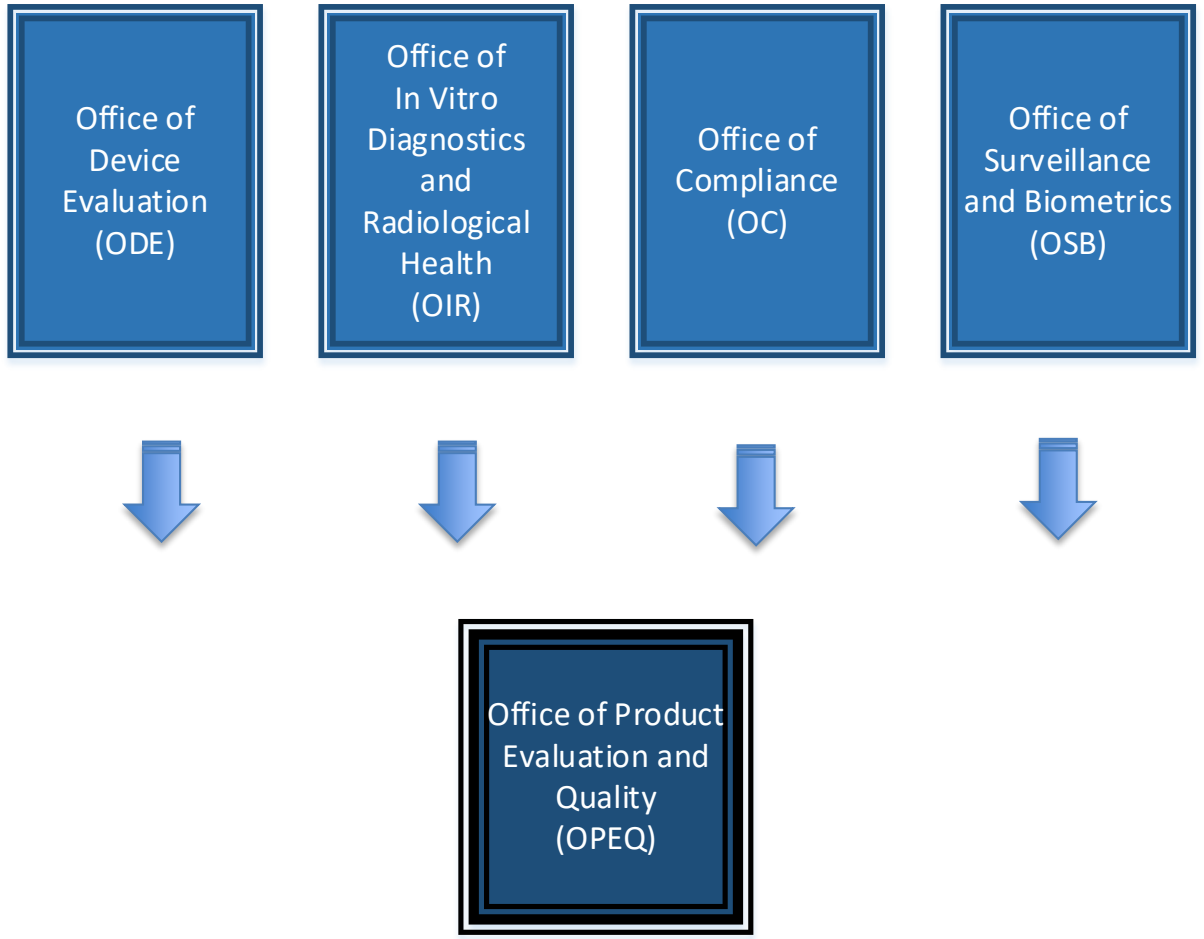


Super Office | Office | Division | Branch | Team | Program/Staff

CDRH Structure After Reorg Implementation

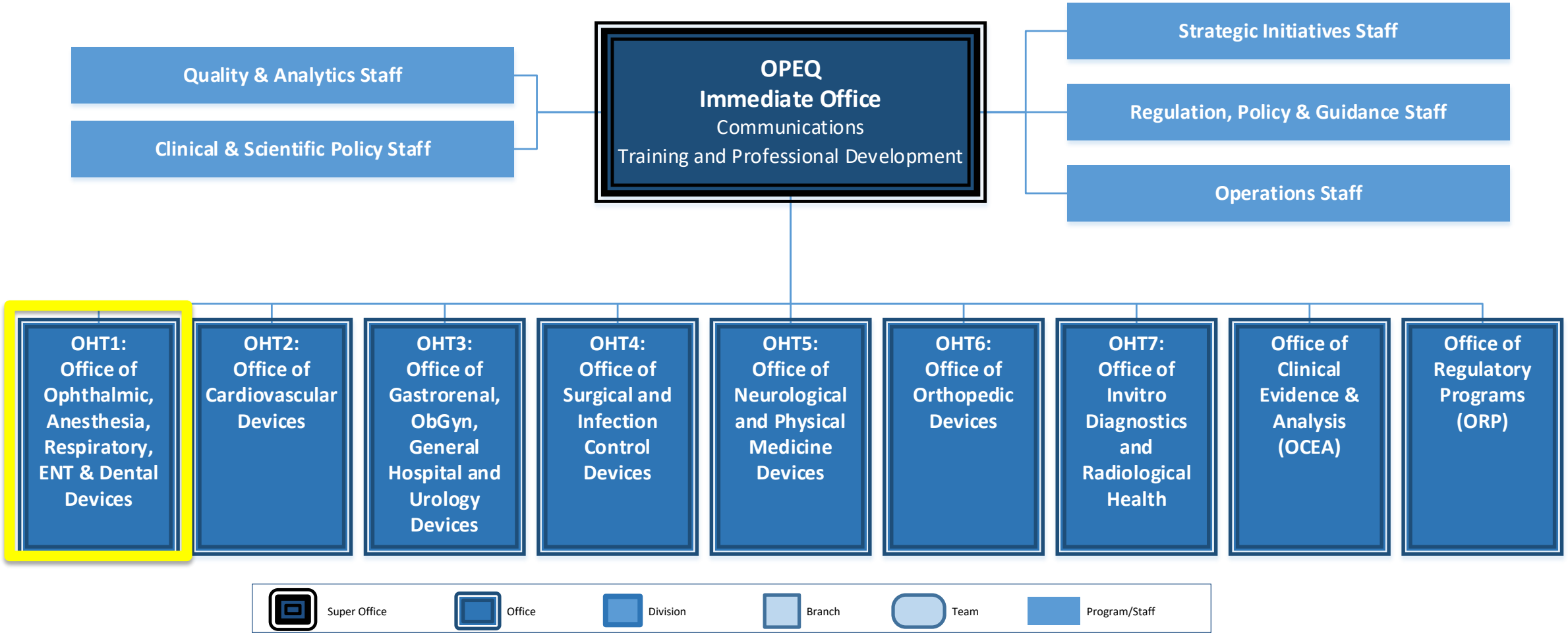


Office of Product Evaluation and Quality

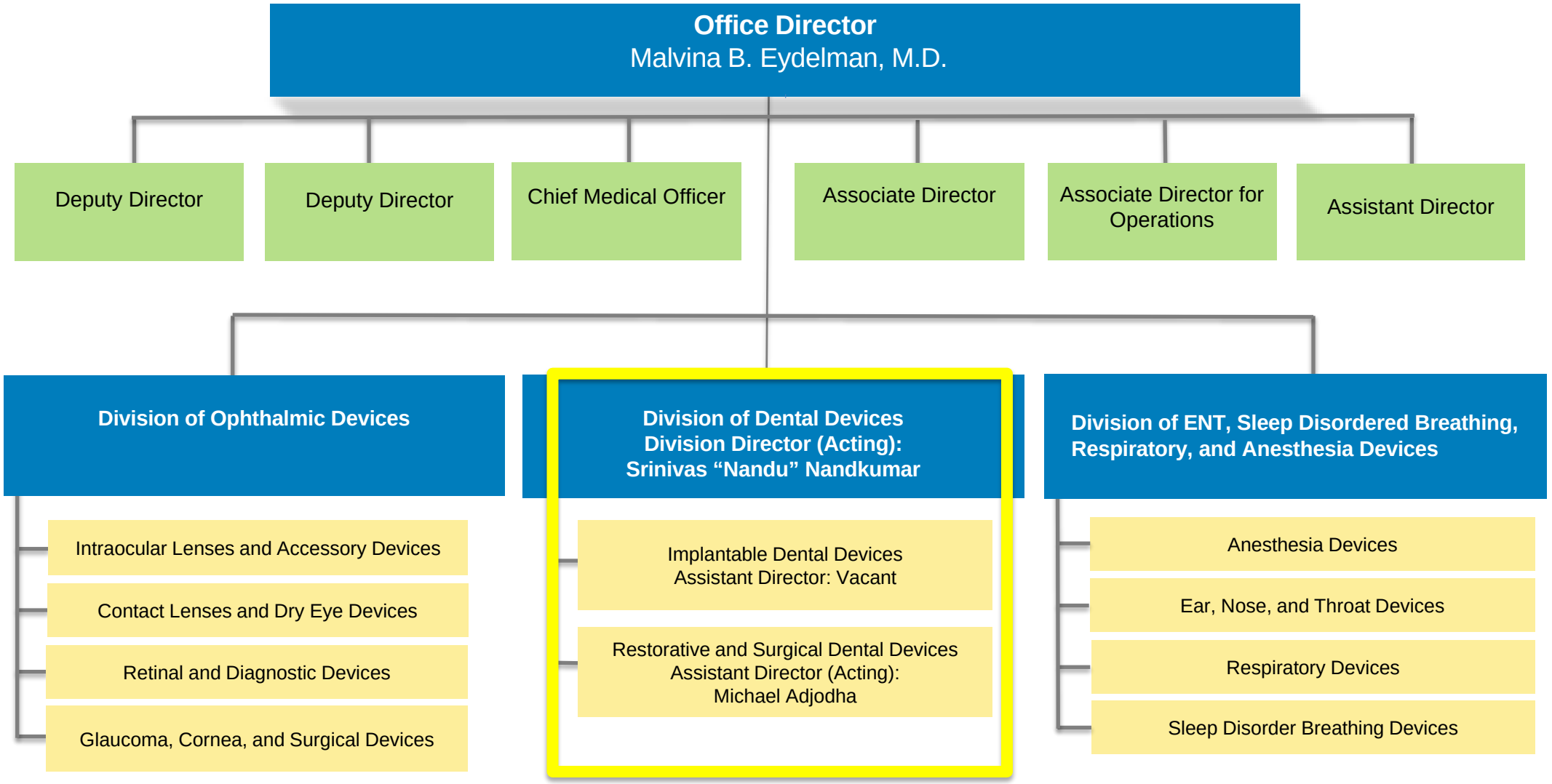


- OC, ODE, OIR, and OSB reorganized into one Super Office (OPEQ)
- OPEQ has 9 offices

Office of Product Evaluation and Quality (OPEQ)



Office of Ophthalmic, Anesthesia, Respiratory, ENT, and Dental Devices (OHT1)



OPEQ Design Features

- Working in teams
  - Team management approach
  - Teams within and across divisions
- Common management chain for compliance, premarket and surveillance programs
- Division is the lowest organizational structure
- Empowering staff by driving decision-making to lowest appropriate level
- Emphasis on professional development & work-life balance

Value Added for You

- Improving our internal processes, coordination and communication → more straightforward & streamlined interactions with CDRH
- Consolidating our structure → provides you with a "one stop shop" in many cases
- Creating a more agile organization → better response to changing regulatory needs and new technologies

Value Added for You

- Ensuring more consistent policy application across OPEQ → easier for you to know what to expect
- Streamlining decision making → more informed interactions with CDRH staff
- Focus on professional growth and creating a better work-life balance for our employees → increased longevity of your points of contact within the organization due to reduced staff turn-over

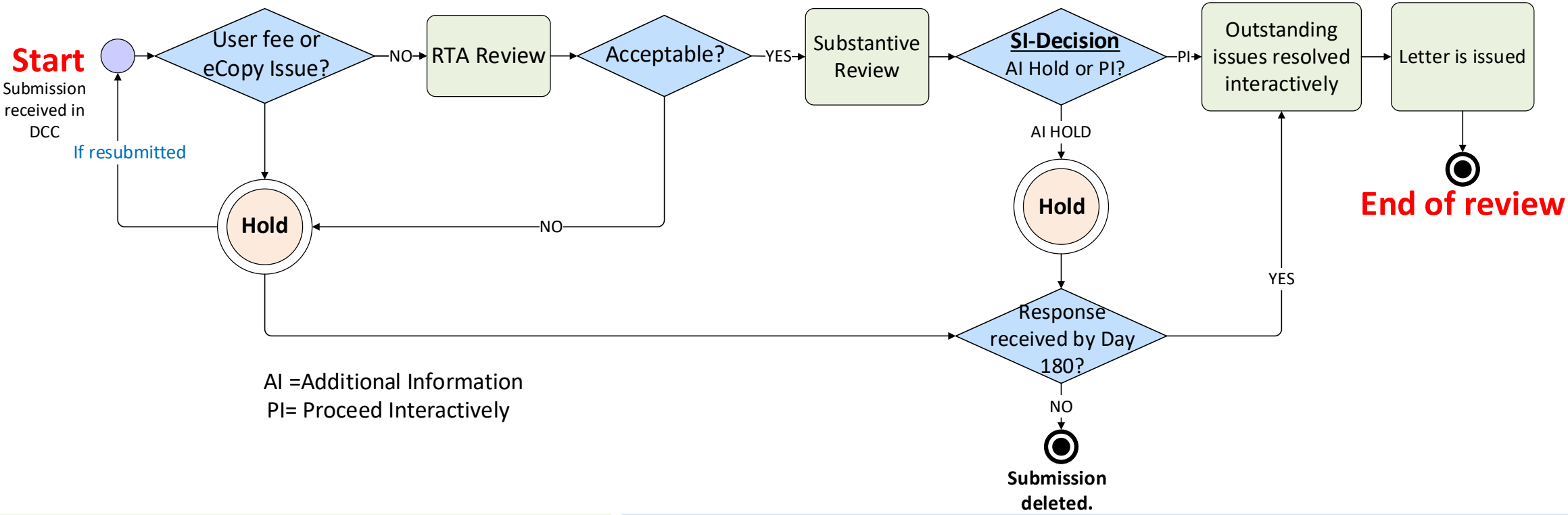
Review Challenges and Opportunities for Dental Device 510(k) Submissions

Michael E. Adjodha, M.ChE.
Acting Assistant Director,
Restorative and Surgical Dental Devices Team

Background

- Each person who wants **to market in the U.S. a medical device** intended for human use (for which a Premarket Approval application (PMA) is not required) must submit **a premarket notification submission (510(k))** to FDA **unless the device is exempt** from 510(k) requirements of the Federal Food, Drug, and Cosmetic Act (the FD&C Act).
- The 510(k) pathway is the **most common pathway** to market for medical devices
- A 510(k) is a premarket submission made to the FDA to demonstrate that the device to be marketed is **as safe and effective**, that is, **substantially equivalent**, to a **legally marketed device** (Section 513(i) of FD&C Act)
- For more details about how to prepare a 510(k) submission, see the relevant guidance document: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/format-traditional-and-abbreviated-510ks

510(k) Process Overview



510(k) Review Timeframe in FDA Days:*

- **TRADITIONAL:** 90
- **ABBREVIATED:** 90
- **SPECIAL:** 30
- **THIRD PARTY**:30

The FDA Review Clock:

- Does not begin if there is a user fee or eCopy issue.
- Starts when there are no user fee or eCopy issues.
- Pauses when submission is on Additional Information (AI) hold.
- Resumes upon receipt of response to AI Letter.
- Stops after recommendation letter is issued.

***FDA Days** are calculated as the number of calendar days between the date the 510(k) was received and the date of a MDUFA decision, excluding the days the submission was on hold for an AI request.

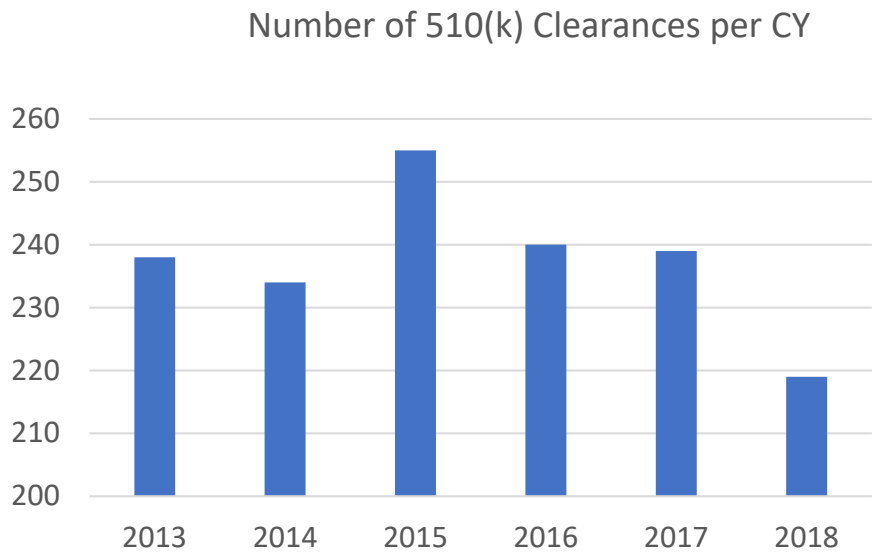
Dental Device Types

Found in Part 872 of Title 21 of the Code of Federal Regulations (21 CFR 872)
www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCFR/CFRSearch.cfm?CFRPart=872

- **Diagnostic Devices**
  - For example, caries detection device, radiography devices, etc.
- **Prosthetic Devices**
  - For example, C&B alloys and resins, composite resins, amalgam, cements, endosseous implants, root canal resins, bone grafting materials, impression materials, denture resins, endodontic materials, etc.
- **Surgical Devices**
  - For example, dental handpieces, ultrasonic scalars, bone plates, etc.
- **Therapeutic Devices**
  - For example, orthodontic appliances and treatment planning software, anti-snoring devices, etc.
- **Miscellaneous Devices**
  - For example, curing lamps, dental operative units, dental ceramics, prophy paste, toothbrushes, etc.

General Observations

- **Predominate workload** involves **510(k)** submissions but also includes **Pre-Submissions**, Premarket Approval **(PMA) supplements** and **30-day notices**, **513(g)** submissions, and Investigational Device Exemptions (**IDEs**)
- **High volume** of 510(k) submissions
  - Significant percentage are from **small or foreign manufacturers**
- **High** first cycle Refuse-to-Accept (**RTA**) rate (81%) in CY 2018
- Average 510(k) clearances: 240+/year, down 10% in CY 2018



General Observations

Device types	Cleared in CY 2018
Dental Abutments (NHA)	66
Endosseous Implants (DZE)	44
Composite Resins (EBF)	18
Aligners (NXC)	11
Snoring/Sleep Devices (LRK)	10
Dental Ceramics (EIH)	10
Resin Bonding Agent (KLE)	9
Dental Handpieces (EFB, EFA, EGS, EKX, EKY)	8
Denture Resin (EBI)	6
Orthodontic Software (PNN)	5

Total cleared in 2018 = 219

General Observations

Device Type	Number of Submissions Accepted in CY 2018	Average FDA Review Days	Average Submitter Days (on hold)	Total Time to Decision
Orthodontic Software	2	90.5	96.5	187.0
Dental Handpieces	8	86.9	87.9	174.8
Snoring/Sleep Devices	12	89.2	54.2	143.4
Endosseous Implants	30	82.4	59.6	142.0
Dental Abutments	15	85.0	45.1	130.1

MDUFA IV				
FY18	FY19	FY20	FY21	FY22
124	120	116	112	108

Refuse-to-Accept (RTA) Challenges

Common challenges include the following elements of the Acceptance Checklist for Traditional 510(k)s:

- **Device Description**
  - Incomplete list and description of each device for which clearance is requested
  - Lack of representative engineering drawings or images of the device
  - Incomplete list (and 510(k) status) of all components of the device and any accessories to be marketed with the device
  - Submission does not address recommendations of device-specific guidance nor provides alternative approach
- **Substantial Equivalence Discussion**
  - Predicate device is used inconsistently; no justification provided if predicate not used in performance testing
  - Lack of an discussion why any differences between your device and the predicate do not impact safety and effectiveness of your device
- **Proposed Labeling**
  - Instructions for use and/or operator manual does not contain indications, a prescription statement (if applicable), and information for professional use, including instructions, hazards, warnings, precautions, contraindications, etc.

RTA Challenges

- **Sterilization**
  - Incomplete information regarding sterilization and reprocessing, including method, validation, sterility assurance level (SAL), packaging, end user instructions, cleaning and disinfection methods
- **Biocompatibility**
  - Lack of biocompatibility testing or rationale on why such testing is not necessary
  - Incomplete material identification of all patient contacting components including all additives; additionally chemical identity should be complete
- **Performance data**
  - Test reports not provided
    - » Sometimes specifications given, no results are provided
  - Irrelevant or inadequate testing that fails to demonstrate how the data supports a finding of substantial equivalence
  - Performance data do not address recommendations of device-specific guidance or provide alternative approach

Substantive Review Challenges and Opportunities

- **Support performance statements with data**
  - Any statement of **device performance** or indication that could **impact** the evaluation of **substantial equivalence** will be evaluated.
  - **New performance statements** will need to be appropriately supported **with data** (e.g. non-clinical performance data); some performance statements may necessitate **clinical data** (e.g. statements regarding **enhanced clinical outcomes**, etc.
- **Select appropriate primary predicate device**
  - Choose a primary predicate device that has the **closest intended use** (1st) and **technological characteristics** (2nd) to your device. Use the 510(k) Premarket Notification database: www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm
  - **Reference devices** can be used for **technological characteristics** (assuming no different Safety and Effectiveness questions) not found in your primary predicate device. See The 510(k) Program guidance (July 28, 2014): www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k

Substantive Review Challenges and Opportunities

- **Irrelevant or inadequate performance data to support a finding of substantial equivalence**
  - Search 510(k) summaries of predicates to determine what tests were relied upon for equivalence
  - Use relevant, recognized consensus standards for performance testing: www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm
  - See guidance on appropriate use of standards: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/appropriate-use-voluntary-consensus-standards-premarket-submissions-medical-devices.
  - Search the guidance documents for appropriate guidance www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance/guidance-documents-medical-devices-and-radiation-emitting-products

- **Biocompatibility**
  - Conduct appropriate testing and/or provide tox risk analysis for why testing is not necessary. See 2016 guidance: www.fda.gov/regulatory-information/search-fda-guidance-documents/use-international-standard-iso-10993-1-biological-evaluation-medical-devices-part-1-evaluation-and

Substantive Review Challenges and Opportunities

- **End user sterilization/reprocessing**
  - Provide **validated instructions** that would allow the user to **properly reprocess the device**.
  - See:
    - 2016 sterility guidance www.fda.gov/regulatory-information/search-fda-guidance-documents/submission-and-review-sterility-information-premarket-notification-510k-submissions-devices-labeled
    - 2015 reprocessing guidance www.fda.gov/regulatory-information/search-fda-guidance-documents/reprocessing-medical-devices-health-care-settings-validation-methods-and-labeling

- **Content of 510(k) summaries should:**
  - **Be complete** per 21 CFR 807.92
  - Include a **comparison of indications and technological characteristics** and why any differences do not affect substantial equivalence
  - Include a brief description of the **tests relied upon** for SE determination
  - Avoid absolute statement that the device is “safe and effective”; 510(k) process is based on substantial equivalence (“**as safe and as effective**”) to a predicate
  - Use the **same Indications** for Use (IFU) in Summary as that in the IFU statement
  - **Not contain trade secret** or confidential commercial information, as it will be posted on the FDA’s public database www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm
  - Follow **good examples** of 510(k) Summaries in the database

Best Practices

- Follow and include a copy of **RTA checklist** in your submission www.fda.gov/medical-devices/premarket-notification-510k/acceptance-checklists-510ks
- **When responding to RTA (or any deficiency)**, please indicate or highlight **how and where** the deficiencies have been addressed
  - See deficiency guidance: www.fda.gov/regulatory-information/search-fda-guidance-documents/developing-and-responding-deficiencies-accordance-least-burdensome-provisions
- Choose an **appropriate predicate device**
  - Search the 510(k) Premarket Notification database www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm
  - See The 510(k) Program guidance www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k

Best Practices

- Include **summary tables of the tests** conducted, even if you include full test reports
  - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/recommended-content-and-format-non-clinical-bench-performance-testing-information-premarket
- Clearly **explain the differences** between your device and the predicate device(s) and **why the differences do not affect** the safety or effectiveness of your device
- Please provide **text-searchable PDF** files
- **Proofread** final submission
  - Ensure **consistency** throughout submission
- Please include your **direct contact information** (email and direct phone line); you may also identify **alternative contacts**, if applicable.

Premarket Resources

- Refer to FDA's **Device Advice** website
  www.fda.gov/medical-devices/device-advice-comprehensive-regulatory-assistance
- **CDRH Learn**
  www.fda.gov/training-and-continuing-education/cdrh-learn
- Division of Industry and Consumer Education (**DICE**)
  www.fda.gov/DICE
- The **510(k) Program** and **Content** guidances
  - www.fda.gov/regulatory-information/search-fda-guidance-documents/510k-program-evaluating-substantial-equivalence-premarket-notifications-510k
  - https://www.fda.gov/regulatory-information/search-fda-guidance-documents/format-traditional-and-abbreviated-510ks
- Consider **Pre-Submissions** for feedback; See the guidance on the Q-Submission Program, www.fda.gov/regulatory-information/search-fda-guidance-documents/requests-feedback-and-meetings-medical-device-submissions-q-submission-program
- Contact the **review division** for additional questions

Reminders

- **Unsupported indications or performance statements** and the selection of **appropriate predicate devices** continue to present the most significant challenges for clearance of dental devices

- Using **relevant guidance/standards** and understanding **the differences between the subject device and predicate device** and clearly articulating and demonstrating how these **do not affect safety and effectiveness** is key to overcoming many deficiencies.

FDA U.S. FOOD & DRUG ADMINISTRATION
CENTER FOR DEVICES & RADIOLOGICAL HEALTH

Postmarket Overview

Srinivas “Nandu” Nandkumar, Ph.D.
Acting Director, Division of Dental Devices

CDRH Vision Statement

"Patients in the U.S. have access to high-quality, safe, and effective medical devices of public health importance first in the world. The U.S. is the world's leader in regulatory science, medical device innovation and manufacturing, and radiation-emitting product safety. ***U.S. post-market surveillance quickly identifies poorly performing devices, accurately characterizes real-world performance, and facilitates device approval or clearance. Devices are legally marketed in the U.S. and remain safe, effective, and of high-quality.*** *Consumers, patients, their caregivers, and providers have access to understandable science-based information about medical devices and use this information to make health care decisions."*

www.fda.gov/about-fda/center-devices-and-radiological-health/cdrh-mission-vision-and-shared-values

Medical Device Reporting (MDR)

- Reports of suspected device-associated deaths, serious injuries, and malfunctions submitted to FDA
- Mandatory reporting by manufacturers, device user facilities, and importers
- Voluntary reporting by health care professionals, patients, and consumers

www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems

FDA's Medical Device Safety Action Plan (November 2018)

"Ensuring that the FDA is consistently first among the world's regulatory agencies to identify and act upon safety signals related to medical devices."

www.fda.gov/news-events/press-announcements/statement-fda-commissioner-scott-gottlieb-md-and-jeff-shuren-md-director-center-devices-and-2

What is a Safety Signal?

- A signal represents information which:
  - may arise from one or more sources
  - suggests a new potentially causal association, or a new aspect of a known association, between a medical device and an event or set of related events
  - might justify or require further evaluation and/or action by the Center
- Examples:
  - Unanticipated/unlabeled adverse events of clinical significance
  - Increase in the severity or rate of a labeled/known event
  - New product failure mechanism/mode causing patient injury
  - Poor outcomes due to inadequate training, inadequate instructions or human factor concerns
  - New risks introduced by off-label use

www.fda.gov/regulatory-information/search-fda-guidance-documents/public-notification-emerging-postmarket-medical-device-signals-emerging-signals

Signal Detection

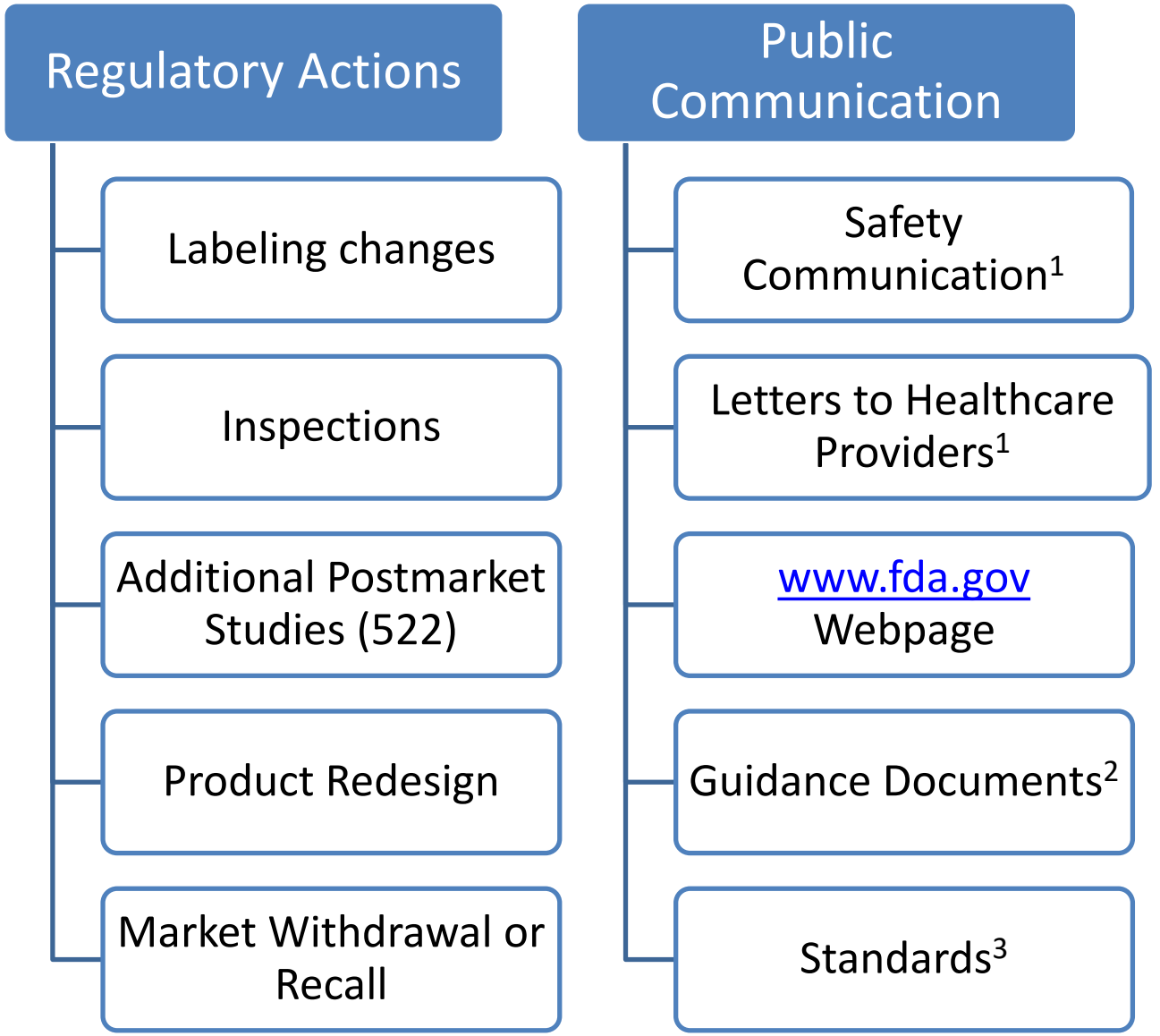
- Medical Device Reports (MDR)[1]
- Post Approval Studies[2]
- 522 Postmarket Surveillance Studies[3]
- Device annual reports
- Consumer complaints

[1] www.fda.gov/medical-devices/medical-device-safety/medical-device-reporting-mdr-how-report-medical-device-problems
[2] www.fda.gov/devicepostapproval
[3] www.fda.gov/522studies

Signal Refinement

- Information Gathering
  - Communication with manufacturer as soon as possible
  - Literature Search
  - Medical Device Report (MDR) Analysis
  - Interim results from ongoing postmarket studies
- Assessment of Signal by Signal Team
  - Likelihood, magnitude, of event
  - Causal relationship
  - Potential for mitigation or alternative therapies

Action Plan



1 https://www.fda.gov/medical-devices/medical-device-safety
2 https://www.fda.gov/regulatory-information/search-fda-guidance-documents
3 https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfStandards/search.cfm

Market Withdrawals and Recalls

- Market Withdrawal: when a manufacturer makes a business decision to withdraw a device from the market for any reason
- Recall: when a manufacturer takes a correction or removal action to address a problem with a medical device, in the field, that violates FDA regulations.
  - Correction vs. removal actions
  - Classification of recalls based on risk to health
- Posted in the online Medical Device Recall Database: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfres/res.cfm

Questions?

Division of Industry and Consumer Education:
DICE@fda.hhs.gov

Slide Presentation, Transcript and Webinar Recording will be available at:

http://www.fda.gov/training/cdrhlearn

Under Heading: Specialty Technical Topics;
Subheading: Device Specific Topics

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immediately following the conclusion of the live webinar.