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Understanding the FDA: Accelerating the Pathway to Approval for Point-of-Care Technologies
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Agenda

- FDA's Regulatory Framework
  - In Vitro Diagnostic Tests (IVDs)
  - Regulatory Pathways
- FDA Applications and Data Requirements
- Special Considerations
  - Point of Care IVDs
  - CLIA Categorization and Waiver
  - Software as a Medical Device
- FDA's Pre-submission Program
- References

- FDA’s Regulatory Framework

Definition of Medical Devices

- A device is an "instrument, apparatus, implement, machine, implant, in vitro reagent, or other similar or related article, including any component, part or accessory, which is –
  - (1) recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
  - **(2) *intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals,* or**
  - (3) intended to affect the structure or any function of the body of man or other animals, and which does not achieve its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its principal intended purpose.

FDA Regulation of IVDs as Medical Devices

- FDA regulates *in vitro* diagnostic tests (IVDs) as medical devices
- FDA regulations define IVDs as:

  "those reagents, instruments, and systems intended for use in the diagnosis of disease or other conditions, including a determination of the state of health, in order to cure, mitigate, treat, or prevent disease or its sequelae. Such products are intended for use in the collection, preparation, and examination of specimens taken from the human body." (21 C.F.R. § 809.3(a))

- Depending on the IVD, it may be regulated as a medical device by the Center for Biological Evaluation and Research (CBER) or the Center of Devices and Radiological Health (CDRH)* e.g.,
  - HIV assays regulated by CBER
  - Syphilis regulated by CDRH

*Refer to Intercenter Agreement Between the Center for Biologics Evaluation and Research and the Center for Devices and Radiological Health available at https://www.fda.gov/combination-products/classification-and-jurisdictional-information/intercenter-agreement-between-center-biologics-evaluation-and-research-and-center-devices-and

Regulation of IVDs as Medical Devices

- IVD medical devices are categorized just like other medical devices into three classes (Class I, II, and III), depending on the potential risk the device poses to the patient or user.
- The device class defines the FDA regulatory requirements:
  - ***Class III -- Premarket approval (PMA)***:
    - These devices pose the greatest potential risk to patients/users
    - Class III devices must be approved under a PMA application
    - PMA requires evidence (including clinical data) that the device is safe and effective for its intended use
  - ***Class II – 510(k) clearance***:
    - Generally are marketed under a 510(k) clearance where deemed "substantially equivalent" to another 510(k)-cleared device (a “predicate)
    - Clinical trial data are usually not required (but this is changing in the current regulatory environment, given greater scrutiny of the 510(k) process)
  - ***Class I – Mostly Exempt from FDA premarket review*** and ***from Design Controls***: Pose minimal potential for harm, Class I devices generally must only follow general controls

CDRH Medical Device Regulatory Pathways

- **Premarket Approval for Devices Regulated as Class III**
  - Premarket Approval Application (PMA, 21 C.F.R. Part 814)
  - Safety and Efficacy of Device Must Be Demonstrated
  - Required for Devices That Are Life-Sustaining or Life-Supporting With Novel Intended Uses, Indications, or Principles/Technology
  - PMAs Required for Devices Not Substantially Equivalent to Class I or II Devices
  - Clinical Data is Pivotal to Assess Safety or Efficacy
  - FDA May Seek Review by an Advisory Panel
  - Pre-approval Inspection of Manufacturing Facilities

CDRH Medical Device Regulatory Pathways

- **510(k) Notification for Devices Regulated as Class II or Class I**
  - 510(k) Notice Demonstrates Substantial Equivalence to Class I or Class II Legally Marketed Device (21 C.F.R. 807) based on:
    - Same Intended Use/Similar Indications
    - Principles of Operation and Technical Characteristics Do Not Raise New Questions of Safety or Efficacy When Compared to Predicate
  - Clinical Data Support May Be Needed (about 10 to 15% of 510(k)s filed annually)

De Novo Review – Evaluation of Automatic Class III Designation

- Because of lack of predicate, devices are automatically considered Class III under section 513(f)(1) of the Federal Food, Drug, and Cosmetic Act (FDC Act)

- FDA's de novo process allows for a streamlined reclassification of low risk devices to a Class II or Class I device that have been "automatically" classified into Class III
  - Intended for devices that are novel but low-to-moderate risk for which no predicate is available and where premarket approval (PMA) is not warranted

- De novo pathway[1] typically falls in between 510(k) and PMA in terms of application volume, data requirements, and FDA review time
  - Can petition for de novo after a "not substantially equivalent" decision following 510(k) review; OR
  - Manufacturer can submit Direct De Novo (without first submitting 510(k)) where no predicate device is available

1. 510(k) "de novo" pathway created in 1997 Food and Drug Administration Modernization Act of 1997 ("FDAMA") and updated in 2012 under Food and Drug Administration Safety and Innovation Act (FDASIA) to create a direct de novo pathway

De Novo Review -- Evaluation of Automatic Class III Designation

- Whether a device is considered low risk, is almost entirely within the discretion of FDA. For example, one of the factors in determining the risk presented by a diagnostic test is the risk resulting from a false positive or false negative result.

- FDA OIVD group also has considered moderate risk devices for de novo classification.

- Manufacturers who believe that their device may qualify for de novo down-classification have a much greater likelihood of success if they discuss the proposed regulatory approach with FDA before submitting a de novo application for the new device.

Indications for Use

- Different claims for same device may affect regulatory pathway – could be 510(k) or PMA
- For example, an IVD that detects a tumor associated antigen:
  - As a screening test to detect cancer – PMA
  - As a monitoring test to assess response to therapy or recurrence – 510(k)

- FDA Applications and Data Requirements

What Type of Supportive Studies are Required for IVDs in FDA Premarketing Submissions?

- *Studies that support the IVDs Indications for Use*
  - *Analytical Performance Characterization Studies*
  - *Method Comparison Studies* –
    - An IVD device that uses a well-characterized technology and has an intended use that falls within a type of device that has been classified into Class I or Class II may only require a comparison of analytic performance to that of a legally marketed (i.e., predicate) device.
- *Clinical Studies* –
  - If the IVD uses novel or unproven technology or has a new intended use or new indications, FDA has often requested a well-planned clinical study of the device in the intended use target population.
  - Required for de novo and PMA applications

Analytical Performance Characterization of IVDs

- Examples of Analytical Studies
  - Detection Limits
  - Precision/Reproducibility
  - Accuracy
  - Linearity
  - Interference
  - Cross-reactivity
  - Analytical Specificity
  - Stability
- The type of testing depends on the intended use and analytical characteristics.
- Expectation, where practical, study designs should follow CLSI* FDA Recognized Consensus Standards study designs

*Clinical Laboratory Standards Institute

Clinical Trial Data for IVDs – U.S.

- Determinants on the need for or type of clinical evidence to support premarket submissions include:
  - Intended use of the IVD
  - The type and amount of published clinical evidence that is germane to the intended use
  - FDA's knowledge and experience with the device's technology

FDA's Guidance for Industry and FDA Staff *In Vitro Diagnostic (IVD) Device Studies – Frequently Asked Questions* (June 25, 2010) (FDA's IVD Study FAQ Guidance)

Clinical Trial Data for IVDs – U.S.

- Clinical data typically required when the IVD has
  - New intended uses or possibly new indications
  - Novel technology,
  - May change the standard of care algorithm change
    - Go from adjunctive use to stand alone use
  - Predicate device uncertainty

- Pre-IDE discussions with FDA are essential to understand study expectations for clinical support

- Special Considerations

Point of Care (POC)

- POC Diagnostic Testing Definition
  - Testing performed near a patient or by a patient
  - Outside the testing of a centralized laboratory testing facility
  - Not intended to refer to sample collection procedures only

- Types of POC Tests
  - Home use
  - Over-the-counter
  - Doctor's offices and clinics
  - Patient bedside

Examples of 510(k)-cleared POCs

- Abbott i-STAT Alinity system with Hematocrit test (k163342) and Glucose test (k163271)
- Roche Cobas 101 system with HbA1c test (k163633)
- Instrument Laboratory GEM Premier 5000 with electrolytes (k160225), blood gas (k160412), glucose, lactate, tBili (k160402), hematocrits, tHb, etc. (k160415)
- Sysmex XW-100 Automated Hematology Analyzer (K143577)

POC Testing Settings

- POC include both CLIA waived or moderate complexity tests*

	POC (Type 1)	POC (Type 2)	POC (Type 3)	CENTRAL LAB
Healthcare Setting	Doctor's Office	Small Lab (group of MDs)	Medical Institution	
			ER, OR, Bed-side	Hospital Lab
Relative to Patient	(Near Patient)	(Near Patient)	(Near Patient)	(Away from Patient)
Type of Testing (CLIA Complexity)	**Waived**	**Non-waived** (Moderate Complexity)	**Non-waived** (Usually Moderate Complexity)	**Non-waived** High and Moderate Complexity
CLIA Certificate	CLIA Waived	Certificate of Compliance	Certificate of Compliance	
Operators (Testing Staff)	Nurses, Doctors, PAs, Office Staff	Professional Laboratory Staff (lower education requirements)	Trained Nurses Professional Laboratory Staff	Professional Laboratory Staff

*FDA April 10, 2019, *Successful Submissions for Point-of-Care (POC) IVDs,* AMDM 46th Annual Meeting, April 2019.

POC Studies

- In addition to the prior examples of analytical studies listed, Method Comparison and Precision Studies must be conducted at POC sites.
  - ***Method Comparison***
    - A minimum of three testing sites representative of different intended-use, near-patient care environments
    - Test operators should represent intended users
    - The same comparator is used for all study samples
    - POC sites in the United States
  - ***Precision***
    - A minimum of 3 POC sites with a minimum of 2 POC operators at each POC site
    - Test sample panel used across all POC sites
- Study sites should be diverse enough to represent the intended use settings (e.g., doctor office, clinic, bedside, ER, etc.)

POC IVDs

- FDA clearance or approval does not mean the POC is CLIA waived.

- CLIA Waiver applications require other information and studies such as use with untrained operators.

CLIA Categorization and Waiver

- CLIA regulations (42 C.F.R. Part 493) require laboratories to meet certain standards for quality systems, personnel, test method verification, calibration, proficiency testing, record keeping, and certification.
  - With few exceptions, a lab must apply for and obtain CLIA certification before accepting materials derived from the human body for the purpose of providing information for the diagnosis, prevention, or treatment of any disease or the impairment of, or assessment of, human health
    - Includes waived tests designated for use at "point-of-care" settings in hospitals, physicians' offices, and clinics
- FDA is responsible for categorizing IVD tests into one of the three designated groups of CLIA complexity:
  - Waived
  - Moderate complexity
  - High complexity
- FDA determines CLIA categorization by review of the package insert test instructions in the premarket submission (see 42 C.F.R. 493.17)
  - Occurs in parallel to the premarket review if the test is regulated under CDRH and immediately after if it is regulated under a different FDA Center e.g., CBER

CLIA Categorization and Waiver

- **CLIA Waiver by Regulation** [42 C.F.R. § 493.15(c)] -
  - Dipstick or Tablet Reagent Urinalysis (non-automated) for bilirubin, glucose, hemoglobin, ketone, leukocytes, nitrite, pH, protein, specific gravity, or urobilinogen;
  - Fecal occult blood tests (non-automated);
  - Ovulation tests using visual color comparison for human luteinizing hormone;
  - Urine pregnancy tests using visual color comparison;
  - Erythrocyte sedimentation rate (non-automated);
  - Hemoglobin – copper sulfate (non-automated);
  - Blood glucose by glucose monitoring devices cleared by FDA for home use;
  - Spun microhematocrit; and
  - Hemoglobin by single analyte instruments with self-contained or component features to perform specimen/reagent interaction, providing direct measurement and readout.

- **Home Use and Over-the-Counter (OTC) are automatically granted CLIA Waiver**

CLIA Categorization and Waiver

- **Automatic CLIA Waiver**
  - Tests systems that involve simple examinations and procedures which are FDA cleared or approved for over-the-counter (OTC) use or for prescription home use (e.g., prothrombin, cholesterol, alcohol, etc.)
- **Dual Submission** pathway created in 2012 – CLIA Waiver occurs simultaneously with a 510(k) notice
- **CLIA Waiver by Application** – occurs after an IVD premarketing submission has been cleared or approved or for tests that are exempt from
  - Tests exempt from premarket notification[1]
  - Tests that were 510(k)-cleared or PMA-approved and originally categorized as moderate complexity[2], if the manufacturer believes the statutory criteria for waiver can be met.

1. Limitations of device exemption 21 CFR xxx.9 , for example such as near patient testing (point of care) where a 510(k) may be required. FDA would recommend a Dual Submission in this case.
2. Tests that have been previously categorized as high complexity likely would not be sufficiently “simple” to be waived . Any device modifications made for a simple design would require new 510(k)/PMA approval.

CLIA Categorization and Waiver

- CLIA Waived Tests are defined by the CLIA regulations as those tests that involve simple laboratory examinations and procedures which:
  - Are cleared by FDA for **home use**
  - employ methodologies that are "so **simple and accurate as to render the likelihood of erroneous results negligible**"; or
  - "pose no reasonable risk of harm to the patient if the test is performed incorrectly".

  42 CFR § 493.15 (b).
- FDA expects CLIA-waived tests to be more robust than those tests used by laboratory professionals.
  - In accordance with FDA's current position, test performance that suffices to obtain 510(k) clearance may not meet the threshold for CLIA waiver status

CLIA Categorization and Waiver

- FDA has described characteristics of simple test
  - Is fully automated, unitized, or a self-contained test;
  - Uses unprocessed specimens (e.g., finger stick blood, venous whole blood, urine, nasal swabs)
  - Uses only basic, non-technique-dependent specimen and reagent manipulation (e.g., “mix reagent A and reagent B”; “add buffer to test cartridge”)
  - Requires no operator intervention during the analysis steps;
  - Requires no technical/specialized training for troubleshooting or interpretation of multiple/complex error codes;
  - Needs no electronic or mechanical maintenance beyond simple tasks (e.g., changing a battery);
  - Produces results that require no operator calibration, interpretation, or calculation;
  - Produces results that are clear to read (e.g., “+” or “-”, a direct readout of numerical values, clear presence/absence of a line, or obvious color gradations);
  - Provides instructions for obtaining and shipping specimens for confirmation testing, where clinically advisable; and
  - Includes a quick reference instruction sheet that is written at no higher than a 7th grade reading level.

CLIA Categorization and Waiver

- **Current Recommendations:**
  - Show that the test system design is robust (*i.e.,* insensitive to environmental and usage variation) and that all known sources of error are effectively controlled.
    - **Comprehensive risk analysis and flex studies:** identify and assess potential sources of errors (e.g., system failure, operator error, specimen integrity, environmental factors)
    - **Risk control:** Implement appropriate measures to reduce associated risks, and verify their proper implementation and efficacy
      - Internal controls (*e.g.,* failure alerts and fail-safe mechanisms incorporated into the design, such as lock-out functions that preclude output of results if system checks are not completed or the device was mishandled)
      - External controls (e.g., supply quality control materials that can be easily employed by the operator, along with corresponding instructions, to ensure high levels of accuracy)
    - **Proof:** Verify/validate the insensitivity of the test system to variation under stress conditions and the effectiveness of control measures at operational limits

CLIA Categorization and Waiver

- "Accurate tests" are those that perform comparably to a traceable reference method (or alternate method discussed with FDA), as demonstrated by studies in which intended operators perform the test.
  - In some cases, another method with known accuracy can be used as the comparator
- "Accuracy" is demonstrated through prospective studies comparing the test for which a CLIA waiver is being pursued (Waived Method, or WM) to the traceable comparative method (CM).
  - Such testing should use patient samples collected in the intended testing environment (*e.g.,* operators, conditions of use)
  - IRB approval and informed consent required per 21 C.F.R. Parts 50 and 56
- This clinical design and analysis are influenced by the candidate test and whether it is considered to be a quantitative, semi-quantitative or qualitative as defined below:
  - Quantitative assays and semi-quantitative assays → results express a numerical amount or ordinal categories (e.g., urine test strips that report negative, trace, +, ++, +++)
  - Qualitative assays → provide only two responses (*i.e.,* positive/negative or yes/no or present/absent)

CLIA Categorization and Waiver

- January 2008 guidance, *Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices*
  - Reflects FDA's current thinking regarding how manufacturers can demonstrate that their tests meet the requirements for obtaining a CLIA waiver.
- **Draft Guidance**
  - November 29, 2018, draft guidance, *Select Updates for Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices was issued as a result of the 21st Century Cures Act requiring FDA to the particular section of its 2008 CLIA Waiver Guidance* (Section V. Demonstrating Insignificant Risk of an Erroneous Result – Accuracy).
    - Provides FDA's thinking on use of comparable performance between a waived user and a moderately complex laboratory user to demonstrate accuracy
    - Provides general approaches for study design options for demonstrating accuracy as well as comparable performance to meet CLIA Waiver requirements
    - Incorporates benefit-risk principles in determining "negligible likelihood of erroneous results" in the hands of the waived user recognizing that this will vary from test to test

CLIA Categorization and Waiver

- **CLIA Waiver by Application** (i.e., after a 510(k) clearance has been received) should include:
  - A description of the device demonstrating that it is simple to use
  - Results of risk analysis, including identification of potential sources of errors
  - Results of flex studies demonstrating robustness of design (*i.e.,* that the test system is insensitive to environmental and usage variations under conditions of stress) and operational limitations of the test
  - Results of risk evaluation and control including measures implemented or incorporated into the device to mitigate the risk of errors and verification/validation studies confirming the efficacy of these mechanisms, even under conditions of stress
  - Description of design and results of clinical studies demonstrating insignificant risk of erroneous results when in the hands of the intended user (i.e., accuracy studies)
  - Proposed labeling, including package labeling and instructions for use consistent with a device that is "simple"
- FDA also recommends that a sample of the device be provided, where possible, to aid in the determination of whether it is "simple."*

*It has been in rare occasions that samples of the devices are provided. However, if it is beneficial, to demonstrate simplicity consideration should be given in presenting the device during the pre-submission process.

CLIA Categorization and Waiver

- **Draft Guidance**
  - November 29, 2018, draft guidance, *Recommendations for Dual 510(k) and CLIA Waiver by Application Studies*
    - Describes recommended components of a Dual Submission based on FDA's experience of current submissions to include all elements of a 510(k) submission as well as elements of CLIA Waiver by Application
    - Provides general discussion of comparison and reproducibility study designs for generating data that supports *both* 510(k) clearance and CLIA waived categorization using CLIA Waived operators and sites
      - Comparison studies – use of appropriate comparator method as discussed in FDA-recognized consensus standards (i.e., CLSI standards)
      - Reproducibility studies – recommends use of appropriate FDA recognized consensus standards (i.e., CLSI) for study design and analysis and describes sources of variability to consider

CLIA Categorization and Waiver

- For Dual Submissions (510(k) plus CLIA Waiver categorization), applicants should first inform the FDA that they plan to submit a Dual Submission through a Pre-Submission
  - The Pre-Submission provides a forum for the applicant and FDA to discuss proposed study designs for the Dual Submission.
- Current Dual Submissions have included:
  - Information similar to CLIA by Application
  - Analytical performance characteristics studies to support 510(k) substantial equivalence (SE)
  - Method comparison studies using CLIA-waived sites and operator to support both 510(k) and CLIA Waiver*
  - Reproducibility studies using multiple sites including CLIA-waived sites supporting both CLIA Waiver and 510(k) SE*

*As noted earlier, POC device studies require method comparison and reproducibility studies be conducted at intended POC sites.

CLIA Categorization and Waiver

- **Examples of Recent Dual Submission CLIA-Waived devices include**:
  - **Nova Biomedical StatStrip Glucose Hospital Meter System** (K181043)
    - submitted 04/19/2018
    - 510(k) clearance and CLIA Waiver (CW180005) effective 07/13/2018
  - **Cepheid Gene Xpert Xpress System (Xpert Xpress Strep A**) (K173398)
    - submitted 10/31/2017
    - 510(k) clearance and CLIA Waiver (CW170014) effective on 04/26/2018
  - **Mesa Biotech Accula (Accula Flu A/Flu B Test)** (K171641)
    - submitted 06/02/2017
    - 510(k) clearance and CLIA Waiver (CW170007) effective on 02/06/2018

Software as a Medical Device (SaMD)

21st Century Cures Modifies Device Description

- Modified statutory definition to exclude:

Administrative Software	Health and Wellness	Electronic Health Records	MDDS + Functionality	Clinical Decision Support
Examples •Billing •Scheduling	Must be unrelated to medical purposes	If created by a healthcare provider, and fits within the Health IT certification under section 3001(c)(5) of the Public 20 Health Service Act No analysis functions	Includes lab data and "findings" by a healthcare professional and associated "background information"	Must be transparent and not intended to be the sole basis for a determination. Not analyzing laboratory, imaging or sensor data.

Software as a Medical Device (SaMD)

Clinical Decision Support Tools

- FDA draft guidance, *Clinical and Patient Decision Support Software* (CDS Guidance), issued by FDA in December 2017
  - Interprets Cures Act changes and explains proposed FDA policy for CDS
  - Tools meeting all of the following four criteria are no longer considered devices subject to FDA regulation:
    - *not* intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system;
    - intended to display, analyze, or print medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines);
    - intended for the purpose of supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition; and
    - intended to enable such health care professional to independently review the basis for such recommendations that such software presents so that it is not the intent that such health care professional rely primarily on any of such recommendations to make a clinical diagnosis or treatment decision regarding an individual patient.
  - Also describes proposed policy for Patient Decision Support (PDS) tools

Software as a Medical Device (SaMD)

Draft CDS Guidance

- CDS function is *only* excluded from the definition of a device when it also meets criterion #4
  - i.e., enables independent review of the software's basis for clinical recommendations
  - Health care professional must be able to rely on his/her own judgment, rather than primarily on the software's recommendations, to make clinical decisions for individual patients
  - Requires that the tool clearly explain:
    - its purpose or intended use,
    - the intended user,
    - the inputs used to generate the recommendation (*e.g.*, patient age), and
    - the rationale or support for the recommendation
  - Intended user should be able to reach the same recommendation on his/her own
  - Sources supporting the recommendation or underlying the rationale should be identified, easily accessible, and understandable to the intended user

Software as a Medical Device (SaMD)

Patient Decision Support

- Software intended for use by patients and caregivers who are not healthcare professionals
- Not carved out by the Cures Act, but FDA intends to use enrocement discretion if PDS tools meet the first two Cures Act criteria and:
  - Support or provide recommendations to patients or non-health care professional caregivers, in terms understandable to the intended recipient, about prevention, diagnosis, or treatment of a disease/condition; and
  - Enable the patient or non-health care professional caregiver to independently review the basis for the recommendation so that it is not the intent that such person rely primarily on the recommendation to make a decision regarding a patient.

Software as a Medical Device (SaMD)

FDA General Wellness Guidance

- Enforcement discretion for two categories of products intended only for general wellness:
  - Maintaining or encouraging a general state of health or a healthy activity (now excluded by statute)
  - Associates healthy lifestyle with helping to reduce the risk or impact of a disease/condition
- Only low-risk products - cannot be invasive, pose a risk to user safety, raise novel questions of usability, or raise questions of biocompatibility
- Examples:
  - Product X plays music to relax an individual and "manage stress," without reference to anxiety disorders or any other disease/condition;
  - Software Product Y tracks caloric intake and helps users manage an eating plan to maintain a healthy weight and balanced diet, which may help in living well with high blood pressure and type 2 diabetes;

Software as a Medical Device (SaMD)

FDA Mobile Medical Applications Guidance

- Some "mobile apps" not medical devices. All "mobile medical apps" are medical devices, some are subject to enforcement discretion
- Examples:

Not a Medical Device

- Generic tools like magnifying glass or notes application
- Reference texts
- Educational Materials

Medical Device, but "Subject to Enforcement Discretion"

- Tracking and trending health data for patient's use
- Automate simple tasks for health care providers
- Video games for physical therapy

Actively Regulated Medical Device

- Motion sensor for sleep apnea
- Radiation therapy dose calculation
- Remote display of ICU bedside monitoring data

- FDA’s Pre-submission Program

FDA's Pre-submission Program

- Pre-submission (Pre-Sub) falls under FDA's Q-submission Program
- Voluntary mechanism for seeking guidance concerning product development and/or premarketing submission preparation
- Pre-Sub Process for New Devices (i.e., not yet FDA cleared or approved)
  - Formal written request to FDA requesting feedback from the agency
  - Content of request includes, in part:
    - Device description
    - Intended Use and Indications for Use
    - Summary of any studies conducted to date
    - Proposed analytical and, if necessary, clinical study protocols
    - Submitter's contact information
    - History of any prior FDA interactions
    - Purpose and agenda for interactions
    - List of specific questions for which the submitter is seeking FDA feedback
    - Three (3) or more proposed dates for the interactions
    - List of submitter attendees
- Most effective when requested prior to execution of planned testing.

FDA's Pre-submission Program

- Pre-Sub meeting format can be either a face-to-face meeting or teleconference with FDA.

- Timing:
  - Meeting scheduled approximately 60 to 75 days after receipt of the Pre-Sub by FDA.
  - Written feedback provided approximately 5 days prior to scheduled meeting.

- Submitter required to provide FDA with written minutes of the meeting 15 days after the meeting.

- References

Helpful Links and Guidance

- ***Requests for Feedback and Meetings for Medical Device Submissions: The Q-Submission Program Guidance for Industry and Food and Drug Administration*. May 2019** available at https://www.fda.gov/media/114034/download
- **Search for FDA Guidance Documents** available at https://www.fda.gov/regulatory-information/search-fda-guidance-documents#guidancesearch
- ***De Novo Classification Process (Evaluation of Automatic Class III Designation).* Guidance for Industry and Food and Drug Administration Staff. October 30, 2017** available at https://www.fda.gov/media/72674/download
- **FDA 510(k) Notification Database** available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMN/pmn.cfm
- **FDA Product Code Classification Database** available at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPCD/PCDSimpleSearch.cfm
- **FDA Digital Health Website** available at https://www.fda.gov/medical-devices/digital-health

Helpful Links and Guidance

- **CLIA Waiver by Application Decision Summaries** available at https://www.fda.gov/about-fda/cdrh-transparency/clia-waiver-application-decision-summaries
- ***Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices.*** **Guidance for Industry and Food and Drug Administration Staff. January 30, 2008** available at https://www.fda.gov/media/71069/download
- ***Recommendations for Dual 510(k) and 1 CLIA Waiver by Application Studies.*** **Draft Guidance for Industry and Food and Drug Administration Staff. November 29, 2018** available at https://www.fda.gov/media/109574/download
- ***Select Updates for Recommendations for Clinical Laboratory Improvement Amendments of 1988 (CLIA) Waiver Applications for Manufacturers of In Vitro Diagnostic Devices*****. Draft Guidance for Industry and Food and Drug Administration Staff. November 29, 2018** available at https://www.fda.gov/media/109582/download

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