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January 19	Software As a Medical Device: US FDA Regulatory and Legal Framework
January 20	Patent and Trade Secret Protection for Inventions That Use AI
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February 11	AI in Digital Advisory Offerings: Regulatory Considerations
February 16	Bias Issues and AI

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ARTIFICIAL INTELLIGENCE (AI) BOOT CAMP

Software As a Medical Device: US FDA Regulatory and Legal Framework

Dennis C. Gucciardo
Partner, Washington, DC

Andrew J. Gray IV
Partner, Silicon Valley

January 19, 2021

Biography

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Serving as the leader of Morgan Lewis's semiconductor practice and as a member of the firm's fintech and technology practices, Andrew J. Gray IV concentrates his practice on intellectual property (IP) litigation and prosecution and on strategic IP counseling. Andrew advises both established companies and startups on Blockchain, cryptocurrency, computer, and Internet law issues, financing and transactional matters that involve technology firms, and the sale and licensing of technology. He represents clients in patent, trademark, copyright, and trade secret cases before state and federal trial and appellate courts throughout the United States, before the US Patent and Trademark Office's Patent Trial and Appeal Board, and before the US International Trade Commission.

Biography

Dennis C. Gucciardo
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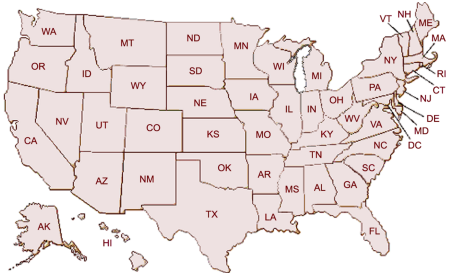
Dennis C. Gucciardo counsels domestic and global medical device manufacturers to help ensure they are operating in compliance with the myriad of US Food and Drug Administration (FDA) regulations, requirements, and expectations. He works with companies—from small startups to large multinational corporations—throughout the product life-cycle on how to bring novel technologies to market, maintain compliance, and avoid FDA enforcement actions.

Dennis helps companies bring medical devices to market, including navigating the premarket process, establishing a quality system, and complying with postmarket requirements. Recently, in response to the coronavirus (COVID-19) global pandemic, Dennis assists companies (traditional medical device manufacturers and new market entrants) with navigating FDA enforcement policies and the Emergency Use Authorization (EUA) process for quickly bringing products to market.

Regulation of Software as a Medical Device in the US

- Food and Drug Administration
- Federal Trade Commission
- State Regulation



FDA's History of Digital Health Regulation

- **1989** – FDA issues Guidance Document, "FDA Policy for the Regulation of Computer Products"
- **2005** – FDA withdraws the 1989 Guidance
- **2008** – FDA issues proposed rule to down-classify "Medical Device Data Systems" or MDDS
- **Late 2009/Early 2010**
  - Inquiries from Senator Charles Grassley (R- Iowa) on potential health IT safety issues and implementation problems
  - Dr. Jeffrey Shuren, Director of FDA's Center for Devices and Radiological Health, stated before the ONC's Health IT Policy Committee: "HIT [health IT] software is a medical device"
- **2011**
  - FDA issues its final rule reclassifying MDDS as Class I
  - FDA issues a new Draft Guidance, "Mobile Medical Applications"
- **2012** – Enactment of the **Food & Drug Administration Safety and Innovation Act (FDASIA)**
- **2013** – FDA finalizes the Mobile Medical App Guidance
- **2014** – FDASIA Health IT Report issued by FDA, ONC, and FCC
- **2015**
  - FDA finalizes its guidance on MDDS and Medical Image Storage/Communication Devices
  - FDA updates the Mobile Medical App Guidance
- **2016**
  - FDA finalizes its guidance, General Wellness: Policy for Low Risk Devices
  - Draft guidance document, Deciding When to Submit a 510(k) for a Software Change to an Existing Device
  - Draft guidance document, Software as a Medical Device (SaMD): Clinical Evaluation
  - Enactment of the **21st Century Cures Act**

FDA's History of Digital Health Regulation

- **2017**
  - FDA announces new Digital Health Innovation Action Plan
  - New draft guidance and final documents on key software issues
- **2018**
  - Draft guidance on Multiple Function Device Products
- **2019**
  - Software Precertification Program – 2019 Test Plan and Working Model 1.0
  - New Discussion Paper on Modifications to AI/ML-based SaMD
  - Six new/updated guidance documents impacting software, including new draft guidance on CDS Software
- **2020**
  - FDA holds Public Workshop on the Evolving Role of Artificial Intelligence in Radiological Imaging to discuss emerging applications of artificial intelligence in radiological imaging, including AI/ML-based devices intended to automate the diagnostic radiology workflow as well as guided image acquisition
  - FDA finalizes its guidance, Multiple Function Device Products: Policy and Considerations
  - COVID-19 enforcement policies
- **2021** - FDA Issues 5-Point Action Plan For Artificial Intelligence/Machine Learning-Based SaMD

When is Software Subject to FDA Regulation as a Medical Device?

- Definition of a Medical Device
- Statutory Exemptions
- Enforcement Discretion Policies and Guidance
- Examples

Scope of FDA Regulation

- FDA regulates software and other technologies that meet the definition of a "device" under the Federal Food, Drug, and Cosmetic Act, which includes
  - Any instrument, apparatus, implement, machine, contrivance, implant, *in vitro* reagent, or other similar related article, including any component, part, or accessory
  - Intended for use in the diagnosis of disease or other conditions, or in the cure, treatment, or prevention of disease, or intended to affect the structure or function of the body
  - Which does not achieve its principal purposes by chemical action in or on the body of man or by being metabolized (*i.e.*, not a drug)

  FFDCA § 201(h), 21 U.S.C. § 321(h)

- VERY broad definition

Scope of FDA Regulation

- A *component* is defined by FDA regulation (21 C.F.R. § 820.3(c)):
  - "any raw material, substance, piece, part, software, firmware, labeling, or assembly which is intended to be included as part of the finished, packaged, and labeled device"
- An *accessory* is defined by FDA guidance:
  - A finished device that is intended to support, supplement, and/or augment the performance of one or more parent devices
  - Generally, accessories are products intended for use with finished medical devices
  - For example, software intended to add color or contrast filters to enhance raw images generated by an imaging device

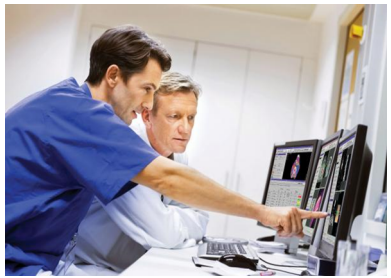
Intended Use

- Authority to regulate revolves around the *intended use*
  - "*Intended for use* in the diagnosis of disease or other conditions, or in the cure, treatment, or prevention of disease, or *intended to* affect the structure or function of the body"
- Your product is what YOU SAY it is
- Intended use is determined by:
  - Claims on the product labels or "labeling" (including websites)
  - Advertising/promotional material
  - Oral or written statements by sales reps
  - Press releases

21st Century Cures Act – Statutory Exemptions

- For *administrative support* functions
  - Includes software for "including the processing and maintenance of financial records, claims or billing information, appointment schedules, business analytics, information about patient populations, admissions, practice and inventory management, analysis of historical claims data to predict future utilization or cost-effectiveness, determination of health benefit eligibility, population health management, and laboratory workflow"
  - Not historically regulated by FDA
- For *maintaining or encouraging a healthy lifestyle*
  - Must be unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition
  - FDA Guidance – General Wellness: Policy for Low Risk Devices

21st Century Cures Act – Statutory Exemptions



- To serve as *electronic health records*
  - Must meet the following criteria:
    - Such records were created, stored, transferred, or reviewed by health care professionals or by individuals working under supervision of such professionals
    - Certified by ONC per Health IT Certification Program (enforcement discretion for non-certified systems)
    - Not intended for interpretation or analysis of patient records or images for the purpose of diagnosis, cure, mitigation, prevention, or treatment of a disease or condition
- For transferring, storing, converting formats, or displaying *medical device data or results* (including clinical lab test data)
  - Includes "medical device data systems" or "MDDS"

21st Century Cures Act – Statutory Exemptions

- For *clinical decision support* (CDS) functions that meet the following criteria:

1. Is not "intended to acquire, process, or analyze a medical image or a signal from an *in vitro* diagnostic device or signal acquisition system"
2. Is intended for the purpose of "displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines)"
3. Is intended for the purpose of "supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition"
4. Is intended for the purpose of "enabling 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"

The CDS exemption only includes software *intended for use by a health care professional* – not for consumer use

Clinical Support Software

- New draft guidance to interpret the statutory exemption for Clinical Decision Support Software
- Second attempt – FDA issued a prior draft in Dec. 2017 that received significant scrutiny
- New draft guidance creates a new broader definition of "CDS" using criteria 1 and 2, and part of criterion 3 from the 21st Century Cures Act:
    1. Not intended to acquire, process, or analyze a medical image or a signal from an *in vitro* diagnostic device or signal acquisition system
    2. Intended to display, analyze, or print medical information about a patient or other medical information
    3. Supports or provides recommendations to the user about prevention, diagnosis, or treatment of a disease or condition

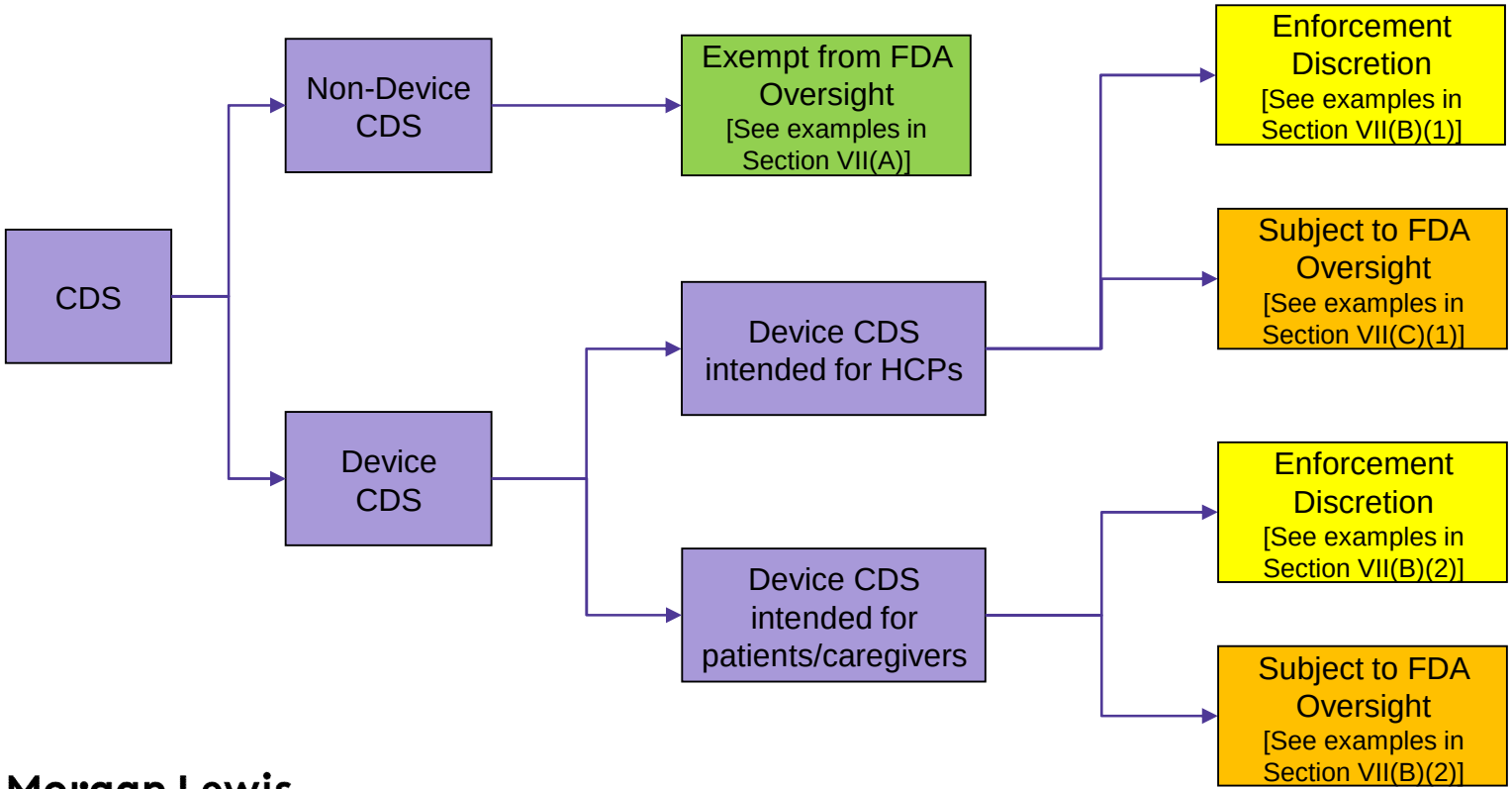
Clinical Support Software

- New draft guidance the breaks down CDS into the following categories:
  - Non-Device CDS:
    - Includes CDS that meets all four criteria under the 21st Century Cures Act and is therefore exempt from FDA regulation
    - Specifically, this includes CDS (as defined on prior slide) that
      - Is intended solely for HCP use
      - Enables the HCP user to independently review the basis for the CDS recommendations
  - Device CDS: Includes CDS that does not meet all four criteria of the statutory exemption
    - Includes CDS that is intended for patient or non-HCP caregiver use
    - Also includes CDS that does not allow the user to independently review the basis for the CDS recommendations (whether the intended user is a patient, caregiver, or HCP)

Clinical Support Software

- For Device CDS, the new draft guidance proposes *policies of enforcement discretion* based on International Medical Device Regulators Forum (IMDRF) risk categorization framework
  - From the IMDRF guidance document, *Software as a Medical Device: Possible Framework for Risk Categorization and Corresponding Consideration*
    - This IMDRF guidance has not been adopted as an FDA guidance, per good guidance practices
    - Also, the IMDRF risk framework differs from the risk framework established under the FFDCA for medical devices
  - To qualify for enforcement discretion, the Device CDS must be intended solely to "inform clinical management" for "non-serious conditions"
  - In addition, Device CDS intended for patient/caregiver use must enable the user to independently review the basis of the CDS recommendations

Clinical Decision Support Software – CDS Flowchart

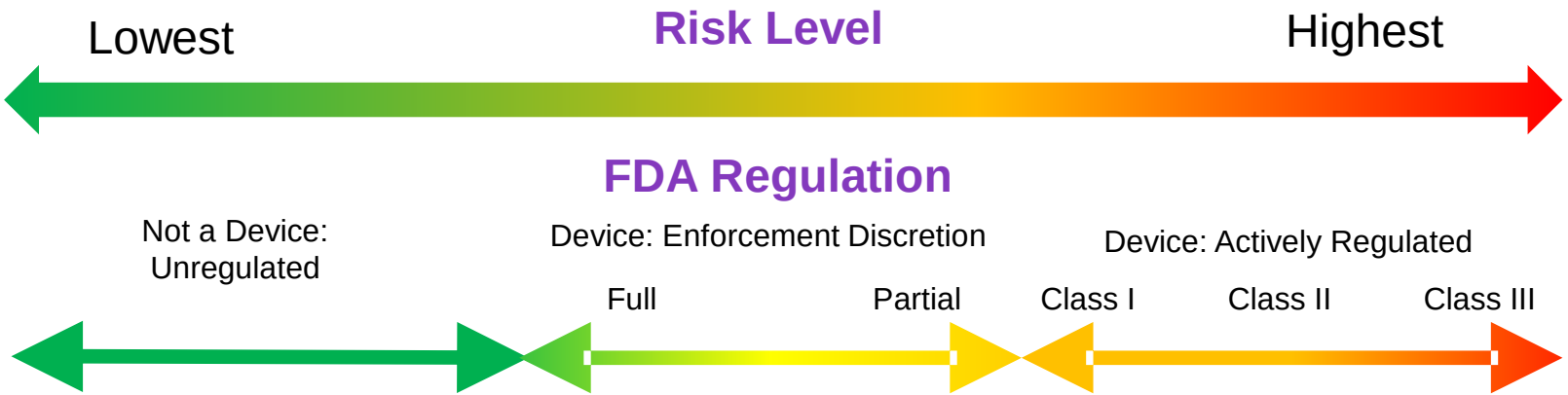


Clinical Decision Support Software – CDS Chart

CDS Type	Non-Device CDS	Device CDS for HCP Use		Device CDS for Patient Use	
Regulatory Status	Exempt from FDA Oversight	Enforcement Discretion	FDA Oversight	Enforcement Discretion	FDA Oversight
21st Century Cures Criteria (See Section V of the Draft Guidance)	Must fully meet all 4 criteria	Must fully meet first 3 criteria	Must fully meet first 3 criteria	Must meet all 4 criteria, except the parts of criteria 3 & 4 limiting CDS to use only by HCPs	Must meet first 3 criteria, except the parts of criterion 3 limiting CDS to use only by HCPs
IMDRF Risk Framework Restrictions	N/A	Must be intended solely to "inform clinical management" for "non-serious conditions"	N/A	Must be intended solely to "inform clinical management" for "non-serious conditions"	N/A
Examples in Draft Guidance	See Section VII(A)	See Section VII(B)(1)	See Section VII(C)(1)	See Section VII(B)(2)	See Section VII(C)(2)

Enforcement Discretion

- FDA may choose not to actively regulate low risk devices under a policy of *enforcement discretion*
- FDA may apply enforcement discretion to exempt certain devices from *all* or *some* of the FDA regulatory requirements (*e.g.*, enforcement discretion for 510(k) requirement only)



Device Software Functions and Mobile Apps

- Updated 2019 to reflect 21st Century Cures Act changes and to cover software on general-purpose computing platforms, in addition to apps intended for use on mobile platforms
- Describes FDA's intent to focus its oversight authority "*only to those software applications whose functionality could pose a risk to a patient's safety if the software applications were to not function as intended*."
- Identifies three categories of software functions:
  - Software functions that FDA intends to regulate as medical devices
  - Software functions that may meet the statutory definition of a "device" but for which FDA intends to exercise enforcement discretion
  - Software functions that do not meet the statutory definition of a "device" and which FDA will not regulate

Device Software Functions and Mobile Apps

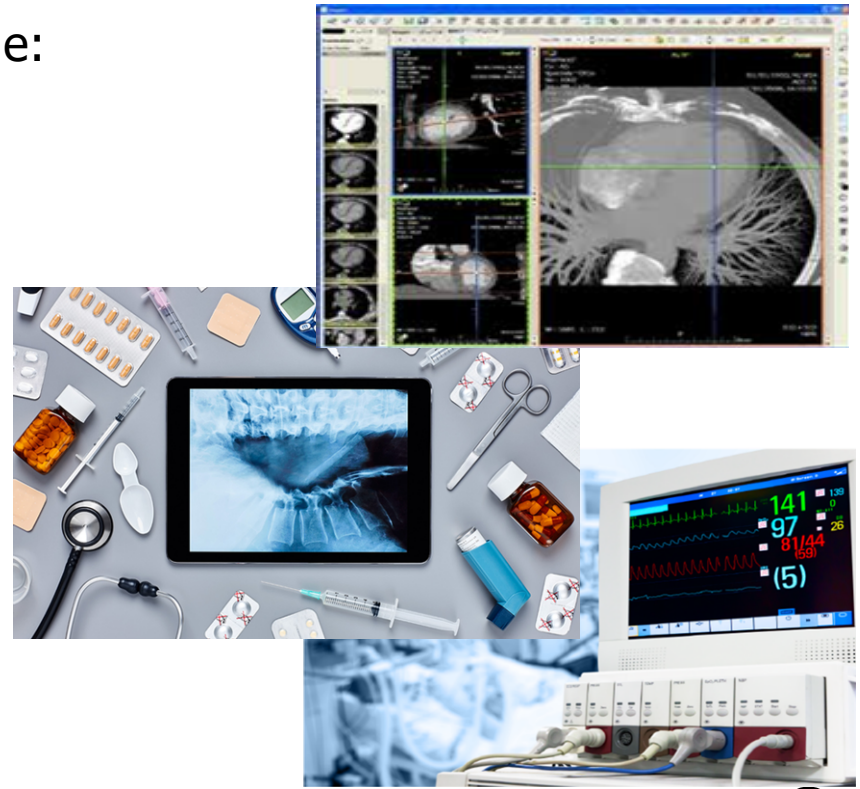
- Regulated Apps:
  - Apps that are an extension of a medical device by connecting to the device for purposes of controlling the device or analyzing medical device data
  - Apps that transform a mobile platform into a regulated medical device
  - Apps that perform patient-specific analysis and provide patient-specific diagnosis or treatment recommendations
- Enforcement discretion:
  - Apps to provide or facilitate supplemental clinical care
  - Apps that provide easy access to information related to the patient's health conditions or treatments
  - Apps that are specifically marketed to help patients communicate with healthcare providers
  - Apps that perform simple calculations routinely used in clinical practice
- Unregulated:
  - Apps that automate general office functions in a healthcare setting
  - Apps used for educational tools for medical training
  - Apps for general patient education or facilitate access to commonly used reference information

MDDS and Medical Image Management Devices

- September 2019 Guidance, updated from 2015 guidance
- Policy of enforcement discretion for the following types of devices:
  - Medical Device Data Systems (MDDS), which provide one or more of the following uses
    - The electronic transfer of medical device data
    - The electronic storage of medical device data
    - The electronic conversion of medical device data from one format to another format in accordance with a preset specification;
    - The electronic display of medical device data
  - Medical Image Communications Devices
  - Medical Image Storage Devices
- 2019 update makes clear that software functions intended for MDDS purposes are exempt per 21st Century Cures Act

MDDS and Medical Image Management Devices

- Limitations on exemption – does not include:
  - Picture Archiving and Communications Systems (PACS)
  - Systems that alter the image data
  - Systems that control or alter the function or parameters of connected medical devices
  - Systems with alarm functions
  - Systems that analyze the medical device data
  - Systems with complex quantitative functions



General Wellness: Policy for Low Risk Devices

- Describes enforcement discretion policy for devices that are intended only for general wellness uses
  1. An intended use that relates to maintaining or encouraging a general state of health or a healthy activity, or
  2. An intended use that relates to the role of a healthy lifestyle with helping to reduce the risk or impact of certain chronic diseases or conditions and where it is well understood and accepted that healthy lifestyle choices may play an important role in health outcomes for the disease or condition
- Includes the following types of claims:
  - Weight management
  - Physical fitness, including recreational use
  - Relaxation or stress management
  - Mental acuity
  - Self-esteem (including devices with cosmetic functions with claims limited to self-esteem)
  - Sleep management
  - Sexual function

General Wellness: Policy for Low Risk Devices

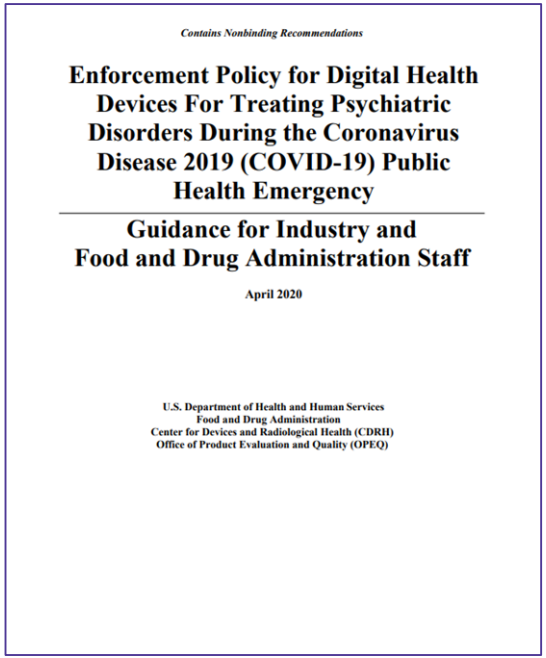
- General wellness devices also must present a very <u>low risk</u>
  1. Is the product invasive?
  2. Is the product implanted?
  3. Does the product involve an intervention or technology that may pose a risk to the safety of users and other persons if specific regulatory controls are not applied, such as risks from lasers or radiation exposure?

FDA COVID-19 Policies for Digital Health

2020 COVID-19 Guidance Documents - Title	Date Issued	Status
Enforcement Policy for Remote Digital Pathology Devices During the COVID-19 Public Health Emergency	04/24/2020	Final
Enforcement Policy for Imaging Systems During the COVID-19 Public Health Emergency	04/23/2020	Final
Enforcement Policy for Non-Invasive Fetal and Maternal Monitoring Devices During the COVID-19 Public Health Emergency	04/23/2020	Final
Enforcement Policy for Telethermographic Systems During the COVID-19 Public Health Emergency	04/16/2020	Final
Enforcement Policy for Digital Health Devices for Treating Psychiatric Disorders During the COVID-19 Public Health Emergency	04/14/2020	Final
Enforcement Policy for Remote Ophthalmic Assessment and Monitoring Devices During the COVID-19 Public Health Emergency	04/06/2020	Final
Enforcement Policy for Clinical Electronic Thermometers the COVID-19 Public Health Emergency	04/04/2020	Final
Enforcement Policy for Non-Invasive Remote Monitoring Devices During the COVID-19 Public Health Emergency	03/20/2020	Final

Enforcement Policy for Digital Health Devices for Treating Psychiatric Disorders

- New enforcement policy applies to:
  1. Class II computerized behavioral therapy devices, intended to provide a computerized version of condition-specific behavioral therapy as an adjunct to clinician supervised outpatient treatment to patients with psychiatric conditions
     - Exempts such devices from most FDA requirements during public health emergency
     - Does not apply to previously cleared devices
  2. Low-risk general wellness and digital health products for mental health or psychiatric conditions



Contains Nonbinding Recommendations

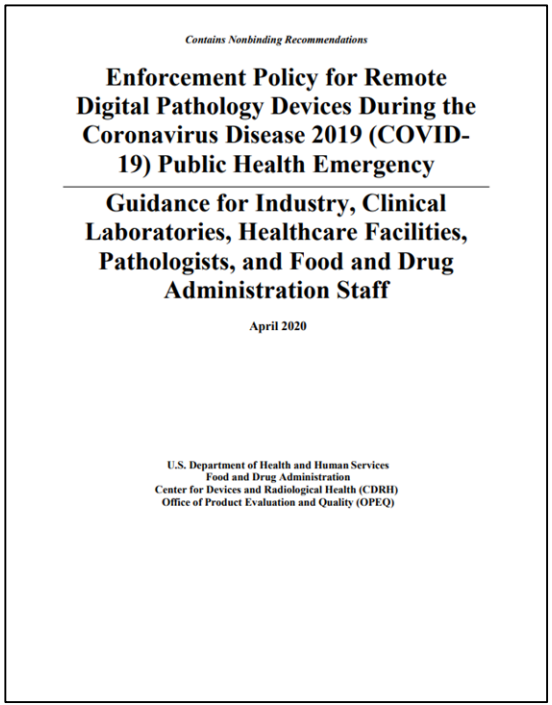
Enforcement Policy for Digital Health Devices For Treating Psychiatric Disorders During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency

Guidance for Industry and Food and Drug Administration Staff

April 2020

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health (CDRH)
Office of Product Evaluation and Quality (OPEQ)

Enforcement Policy for Non-Invasive Remote Monitoring Devices



Contains Nonbinding Recommendations

Enforcement Policy for Remote Digital Pathology Devices During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency

Guidance for Industry, Clinical Laboratories, Healthcare Facilities, Pathologists, and Food and Drug Administration Staff

April 2020

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health (CDRH)
Office of Product Evaluation and Quality (OPEQ)

- Applies to certain Class II digital pathology devices, including:
  - Automated digital image manual interpretation microscope
  - Whole slide imaging system
  - Digital pathology image viewing and management software
  - Digital pathology display
- Guidance covers:
  - Changes to *FDA-cleared devices* – specifically, indications, functionality, hardware and/or software, of digital pathology devices *to provide for use in a remote setting*
  - The marketing of *new digital pathology devices* that are intended for use in remote settings and that are not currently 510(k) cleared for any use
- Must not create "undue risk in light of the public health emergency"

Determining Whether/How Your Software is Regulated as SaMD

- Is it *intended for use* as a medical device?
- Does it fall under an existing *exemption*?
  - Statutory exemptions under the 21st Century Cures Act
  - Enforcement discretion policies per FDA guidance documents
- Does it fall under an existing *classification regulation* or *product code*?
- Have any competitor products been *cleared or approved* by FDA?
- What is the *risk level* associated with the use?

Examples

Unregulated (Not a Device)	Unregulated (Enforcement Discretion)	Regulated
Promotion of machine learning software for medical product research and development	Promotion of software that uses video games to motivate patients to do their physical therapy	Promotion of predictive analytics software for use in analyzing EHR data to predict which patients are most at risk for certain medical events (possibly)
Promotion of software for general purpose electronic health record functions	Promotion of software for transmission and display of medical device data or radiological images	Promotion of clinical app for use in analyzing ophthalmic images to provide diagnosis or treatment recommendations
Promotion of software for use in analyzing billing data to identify potential reimbursement submission errors		

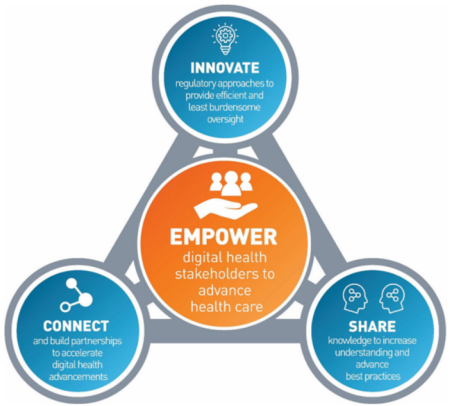
FDA Programs Impacting SaMD

- Digital Health Center for Excellence
- Software Precertification Program
- FDA Discussion Paper – AI/ML Software (2019)
- 5-Point Action Plan For Artificial Intelligence/Machine Learning-Based SaMD (2021)

Digital Health Center for Excellence

- Established **September 22, 2020**
  - "[C]reated to empower stakeholders to advance health care by fostering responsible and high-quality digital health innovation. The DHCoE is part of the planned evolution of the Digital Health Program in CDRH."

Phases	Focus	Activities
Phase 1 (Fall 2020)	Raise Awareness and Engage Stakeholders	• Conduct listening sessions with stakeholders • Develop resources for FDA staff • Begin operationalizing the DHCoE outcome measurement • Amplify FDA's digital health work
Phase 2 (Winter 2020-Winter 2021)	Build Partnerships	• Build strategic partnerships for policy, regulatory science, and fellowships • Develop resources for external stakeholders • Create a digital health community of practice • Assemble FDA and CDRH advisory groups
Phase 3 (Winter 2021 and onward)	Build and Sustain Capacity	• Continue to build strategic partnerships • Update and implement regulatory framework for digital health • Continue harmonization with other regulators



Pre-Certification Program

- **July 2017**: Announce a voluntary pilot program for digital health developers
  - Intended to help FDA gather information and experience in order to create a pre-certification program
  - Nine digital health partners: Apple, Fitbit, Johnson & Johnson, Pear Therapeutics, Phosphorus, Roche, Samsung, Tidepool, Verily
- **April 2018**: FDA issued Working Model (version 0.1) for the pre-certification program
  - Program will be voluntary
  - Current scope limited to Software as a Medical Device

Pre-Certification Program – 2019 Updates

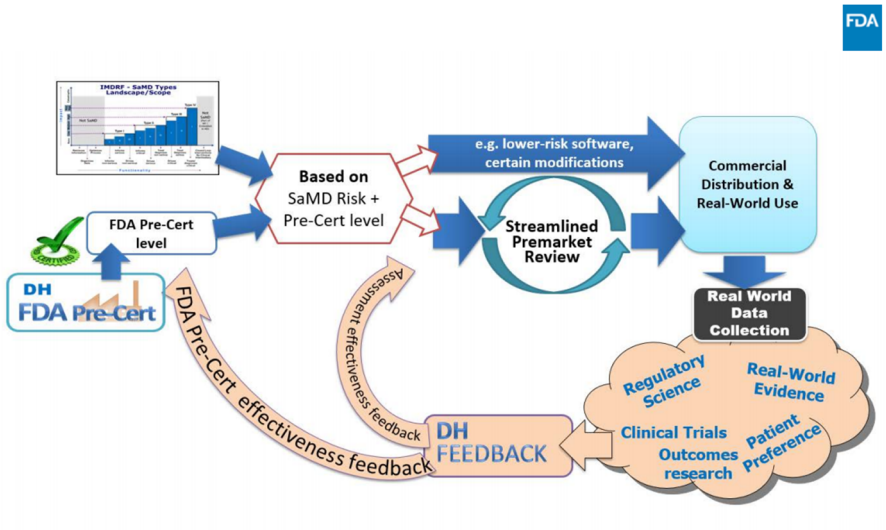


Figure 1. A reimagined approach for the regulation of software

January 2019: FDA issues three new documents:

1. Version 1.0 of the Working Model
2. 2019 Test Plan to Test the Model
   - Internal testing by conducting retrospective tests of SaMD regulatory submissions that were previously reviewed
   - Prospective testing with pilot participants who volunteer to participate
3. Regulatory Framework for Conducting the Pilot Program

Pre-Certification Program – Working Model 1.0

- Four key components:
  - Excellence appraisal and precertification
    - Based on five excellence principles
    - Steps include
      - Pre-Cert Application
      - Appraisal
      - Pre-Cert Status Determination
      - Maintenance and Monitoring
  - Review pathway determination
    - FDA proposes to leverage the risk-category framework for SaMD developed by IMDRF
  - Streamlined premarket review
  - Real-world performance plan
    - Postmarket surveillance and feedback

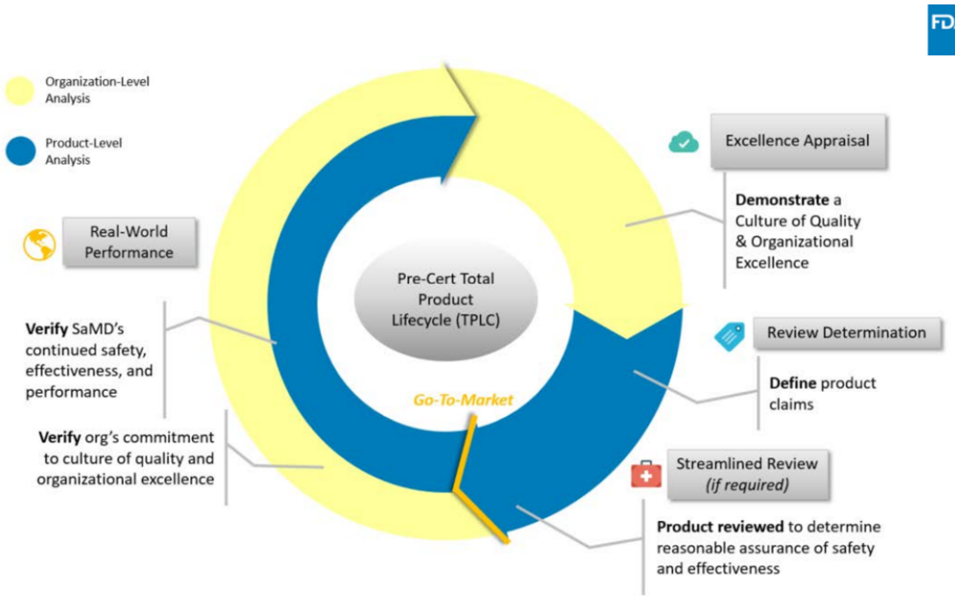


Figure 4. Total Product Lifecycle Approach of the Software Pre-Cert Program

Pre-Certification Program – Excellence Appraisal

Organizational Domains / Excellence Principles	Product Quality	Patient Safety	Clinical Responsibility	Cybersecurity Responsibility	Proactive Culture
1. Leadership & Organizational Support	X	X	X	X	X
2. Transparency	X	X	X	X	X
3. People	X	X	X	X	X
4. Infrastructure and Work Environment	X	X	X	X	X
5. Risk Management	X	X	X	X	X
6. Configuration Management and Change Control	X	X		X	X
7. Measurement Analysis, and Improvement of Processes and Products	X	X	X		X
8. Managing Outsourced Processes, Activities, and Products	X	X		X	X
9. Requirements Management	X	X	X	X	X
10. Design and Development	X	X	X	X	X
11. Verification and Validation	X	X	X		
12. Deployment and Maintenance	X	X	X	X	X

Pre-Certification Program – 2020 Status Update

- FDA continuing to iterate the program based on lessons learned from 2019 Test Plan activities
- "FDA learned that refinements are needed across the program to drive repeatability of the processes, improve the quality and quantity of information, provide clarity to internal and external stakeholders, and reduce the time burden on both internal and external stakeholders."

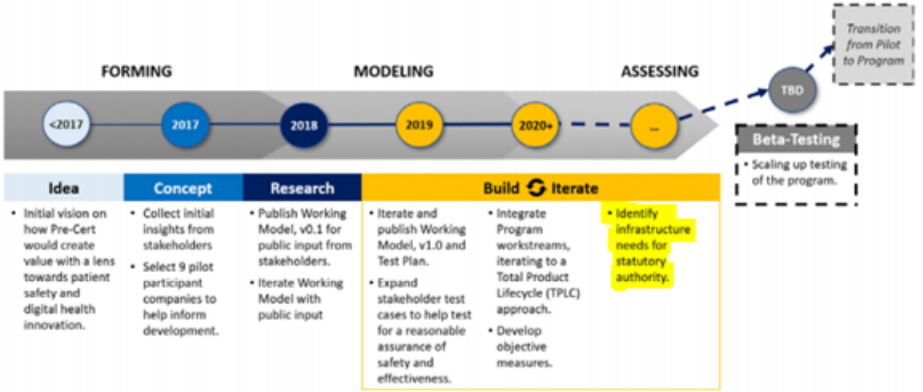
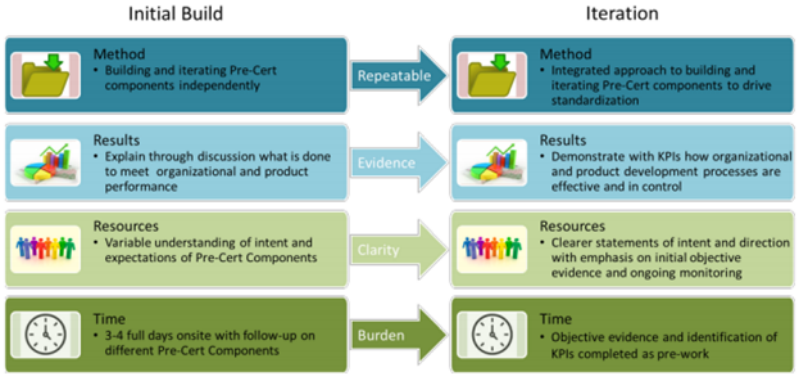


Figure 3. Iterating from Lessons Learned



FDA Discussion Paper - AI/ML Software

- Proposed framework to address how FDA would handle postmarket modifications to AI/ML software devices
  - Existing model for requires sponsors to evaluate all device software changes to determine whether the change requires a new submission to FDA
  - May not work for AI/ML software, because such software is intended to continuously evolve
- Under the proposed framework, AI/ML software developers would include in their initial FDA submissions a predetermined change control plan:
  - SaMD pre-specifications (SPS), which define the types of software algorithm changes that are covered/permitted under the plan
  - Algorithm change protocol (ACP), which defines methods to controls risks for the permitted changes and how the changes may occur
- May require statutory changes to fully implement proposed framework

Proposed Regulatory Framework for Modifications to AI/ML-Based SaMD

1. Changes that fall within the agreed upon SPS + ACP could be documented to file
2. If outside the SPS + ACP and the change leads to a new intended use, change is subject to FDA premarket review
3. If outside the SPS + ACP and no new intended use, change is subject to "focused FDA review"

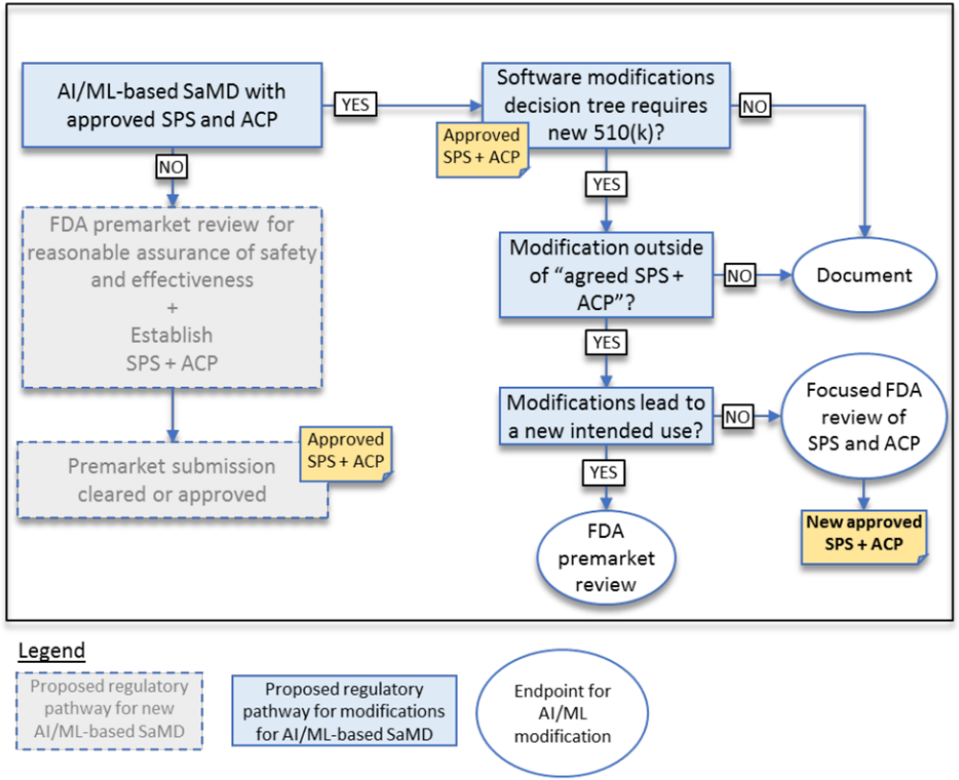


Figure 5: Approach to modifications to previously approved SaMD with SPS and ACP. This flowchart should only be considered in conjunction with the accompanying text in this white paper.

Proposed Regulatory Framework for Modifications to AI/ML-Based SaMD

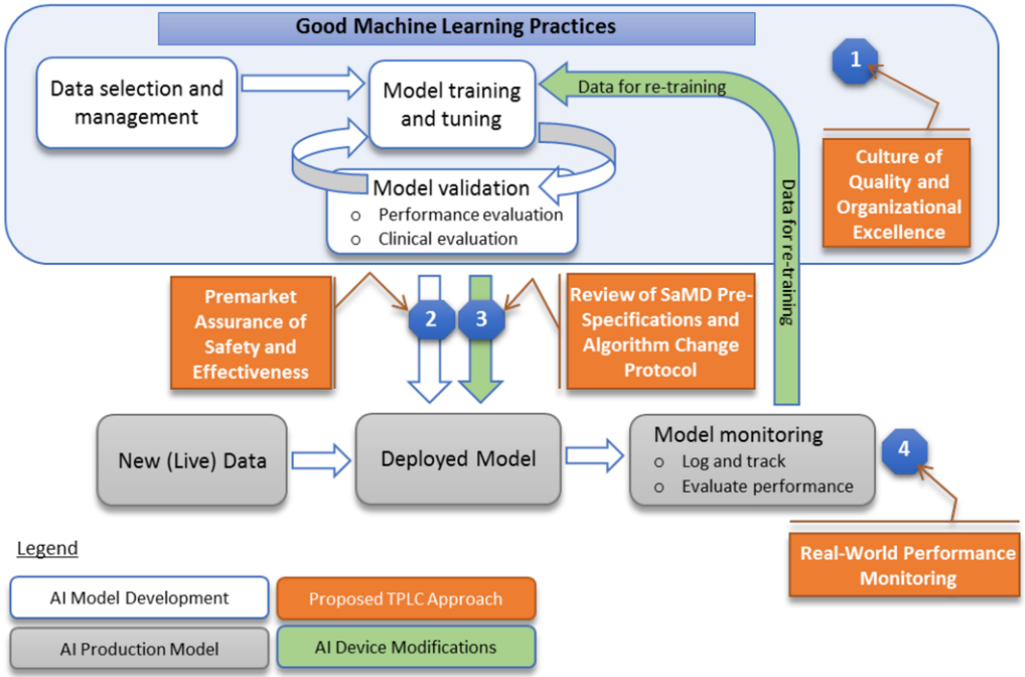


Figure 2: Overlay of FDA's TPLC approach on AI/ML workflow

- Discussion Paper also proposes establishing clear expectations for Good Machine Learning Practices (GMLP) as part of the TPLC approach for AI/ML-based SaMD

Proposed Regulatory Framework for Modifications to AI/ML-Based SaMD

- The Discussion Paper does not define when AI/ML software would be subject to FDA regulation
  - Suggests that certain types of AI/ML software would be regulated – e.g., AI/ML intended to "drive clinical management" or "inform clinical management" or intended for use as "an aid in diagnosis"
  - Specific AI/ML hypothetical examples in Appendix A
    - AI/ML that processes/analyzes physiological signals to detect patterns that occur at the onset of physiological instability and generate alarms
    - AI/ML that uses images taken by a smartphone camera to provide detailed info to dermatologists on physical characteristics of a skin legion
    - AI/ML that analyzes chest x-rays to evaluate feeding tube placement, detect incorrect placements, and triage for radiologists

5-Point Action Plan For Artificial Intelligence/Machine Learning-Based SaMD

Commitment	"Action"	Feedback from 2019 Paper Driving Action
1. Further develop the proposed regulatory framework	Issue draft guidance document (maybe 2021) that will discuss the use of predetermined change control plans (for software learning over time)	• Feedback received showed "strong community interest" in the Predetermined Change Control Plan • Types of modifications to AI/ML software devices proposed in Paper were relevant; however, feedback suggested additional types of modifications that should fall under this framework
2. Support the development of good machine learning practices (GMLP) to evaluate and improve machine learning algorithms	FDA will "deepen" its work in communities in order to encourage consensus outcomes GMLP efforts will be pursued in close collaboration with the Medical Device Cybersecurity Program	• Feedback received generally provided strong support for the idea and importance of GMLP • Request for FDA to encourage harmonization of GMLP with consensus standards efforts, leveraging already-existing workstreams, and involvement of other communities focused on AI/ML

5-Point Action Plan For Artificial Intelligence/Machine Learning-Based SaMD

Commitment	"Action"	Feedback from 2019 Paper Driving Action
3. Foster a patient-centered approach, including device transparency to users	Hold a public workshop to share learnings and to elicit input from the broader community on how device labeling supports transparency to users	• Feedback received indicated concerns with labeling content for AI/ML-based devices: • How to describe the data used to train the algorithm, the relevance of its inputs, the logic it employs (when possible), the role intended to be served by its output, and the evidence of the device's performance • Feedback received indicated that FDA should clarify its position on transparency of AI/ML technology in medical device software
4. Develop methods to evaluate and improve machine learning algorithms.	"Support" regulatory science research efforts to develop methods to evaluate bias in AI/ML-based medical software	• Feedback received described the need for improved methods to evaluate and address algorithmic bias and to promote algorithm robustness

5-Point Action Plan For Artificial Intelligence/Machine Learning-Based SaMD

Commitment	"Action"	Feedback from 2019 Paper Driving Action

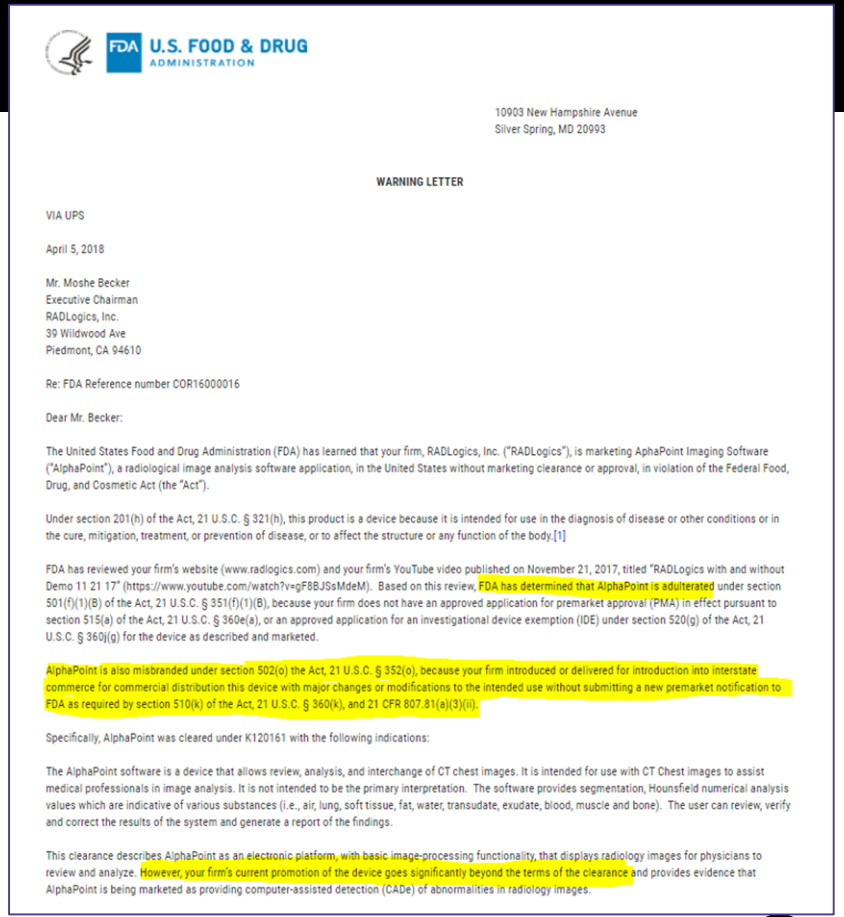
5. Advance real-world performance (RWP) monitoring pilots	Work with stakeholders on a voluntary basis to support RWP monitoring pilots	• Feedback indicated that additional clarity is needed as to the type and nature of RWP data needed to monitor product performance and mitigate risks.
		
		• Questions asked:
		
		  • What type of reference data are appropriate to utilize in measuring the performance of AI/ML software devices in the field?
		  • How much of the oversight should be performed by each stakeholder?
		  • How much data should be provided to the Agency, and how often?
		  • How can the algorithms, models, and claims be validated and tested?
		  • How can feedback from end-users be incorporated into the training and evaluation of AI/ML-based SaMD?

Enforcement for SaMD

- FDA Enforcement Examples
- Federal Trade Commission (FTC) Enforcement Examples
- State Enforcement Examples

FDA Enforcement Examples

- 2018 Warning Letter to RADLogics for promotion of software beyond scope of 510(k) clearance
  - "Language on your firm's website indicates that the AlphaPoint software provides CADe functionality, utilizing machine learning algorithms to automatically detect and mark abnormalities on medical images, including lung nodules, pneumothorax, and pleural effusion"
  - "Your firm's website states that the AlphaPoint software is capable of functioning as a 'Virtual Resident' because it automatically performs an initial review of radiologic images and generates a report listing and characterizing the abnormalities detected in the images, relieving the physician of the task of reviewing the images to identify abnormalities"



FDA U.S. FOOD & DRUG ADMINISTRATION

10903 New Hampshire Avenue
Silver Spring, MD 20993

WARNING LETTER

VIA UPS

April 5, 2018

Mr. Moshe Becker
Executive Chairman
RADLogics, Inc.
39 Wildwood Ave
Piedmont, CA 94610

Re: FDA Reference number COR16000016

Dear Mr. Becker:

The United States Food and Drug Administration (FDA) has learned that your firm, RADLogics, Inc. ("RADLogics"), is marketing AphaPoint Imaging Software ("AlphaPoint"), a radiological image analysis software application, in the United States without marketing clearance or approval, in violation of the Federal Food, Drug, and Cosmetic Act (the "Act").

Under section 201(h) of the Act, 21 U.S.C. § 321(h), this product is a device because it is intended for use in the diagnosis of disease or other conditions or in the cure, mitigation, treatment, or prevention of disease, or to affect the structure or any function of the body.[1]

FDA has reviewed your firm's website (www.radlogics.com) and your firm's YouTube video published on November 21, 2017, titled "RADLogics with and without Demo 11 21 17" (https://www.youtube.com/watch?v=gF8BJSsMdeM). Based on this review, FDA has determined that AlphaPoint is adulterated under section 501(f)(1)(B) of the Act, 21 U.S.C. § 351(f)(1)(B), because your firm does not have an approved application for premarket approval (PMA) in effect pursuant to section 515(a) of the Act, 21 U.S.C. § 360e(a), or an approved application for an investigational device exemption (IDE) under section 520(g) of the Act, 21 U.S.C. § 360j(g) for the device as described and marketed.

AlphaPoint is also misbranded under section 502(o) the Act, 21 U.S.C. § 352(o), because your firm introduced or delivered for introduction into interstate commerce for commercial distribution this device with major changes or modifications to the intended use without submitting a new premarket notification to FDA as required by section 510(k) of the Act, 21 U.S.C. § 360(k), and 21 CFR 807.81(a)(3)(ii).

Specifically, AlphaPoint was cleared under K120161 with the following indications:

The AlphaPoint software is a device that allows review, analysis, and interchange of CT chest images. It is intended for use with CT Chest images to assist medical professionals in image analysis. It is not intended to be the primary interpretation. The software provides segmentation, Hounsfield numerical analysis values which are indicative of various substances (i.e., air, lung, soft tissue, fat, water, transudate, exudate, blood, muscle and bone). The user can review, verify and correct the results of the system and generate a report of the findings.

This clearance describes AlphaPoint as an electronic platform, with basic image-processing functionality, that displays radiology images for physicians to review and analyze. However, your firm's current promotion of the device goes significantly beyond the terms of the clearance and provides evidence that AlphaPoint is being marketed as providing computer-assisted detection (CADe) of abnormalities in radiology images.

Federal Trade Commission Enforcement

- January 2015 complaint against Focus Education, LLC
  - Claims that app permanently improves children's focus, memory, attention, behavior, and/or school performance
  - ADHD claims
- February 2015 actions against MelApp and Mole Detective
  - Claims for analysis of pictures of moles and skin lesions taken with smartphones
  - Melanoma detection claims
- January 2016 complaint against Lumos Labs – Luminosity software
  - Claims to delay memory decline and protect against dementia and Alzheimer's disease
  - Claims to reduce the effects of ADHD and post-traumatic stress disorder
- FTC enforcement thus far is generally consistent with FDA's policies for mobile medical apps and other digital health products

State Enforcement

- New York State Attorney General
  - Developers of three health-related apps
  - Allegations concerning misleading and unsubstantiated claims
  - Irresponsible privacy practices
  - Two of the apps involved were *exempt from FDA regulation*
  - The developers agreed to add new disclaimers, modify their claims, update their privacy policies, and pay a combined $30,000 in penalties

Coronavirus COVID-19 Resources

We have formed a multidisciplinary **Coronavirus/COVID-19 Task Force** to help guide clients through the broad scope of legal issues brought on by this public health challenge.

To help keep you on top of developments as they unfold, we also have launched a resource page on our website at **www.morganlewis.com/topics/coronavirus-covid-19**

If you would like to receive a daily digest of all new updates to the page, please visit the resource page to **subscribe** using the purple "Stay Up to Date" button.

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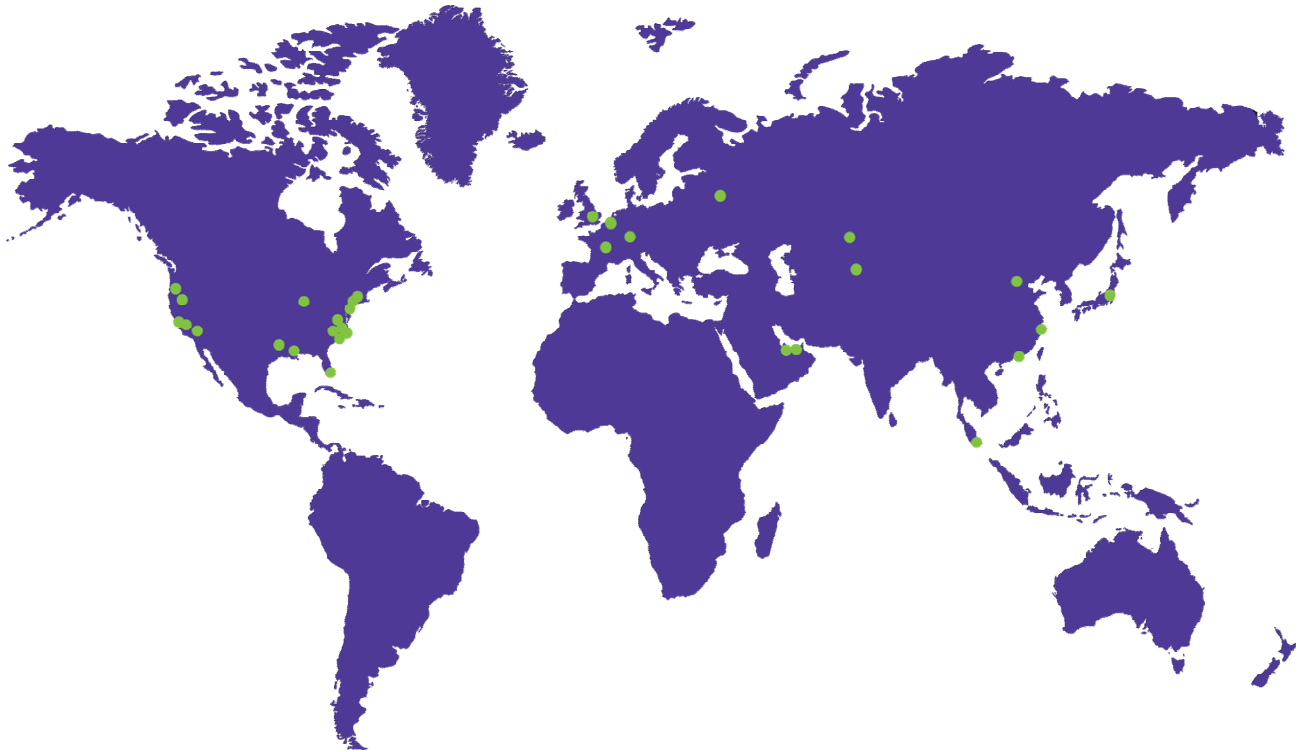

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THANK YOU

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