Morgan Lewis

TECHNOLOGY MARATHON

Digital Health Roundup: FDA Developments and Cybersecurity Considerations

Michele L. Buenafe
Dennis C. Gucciardo

June 9, 2023 |12:00-1:30 pm ET

Presenters

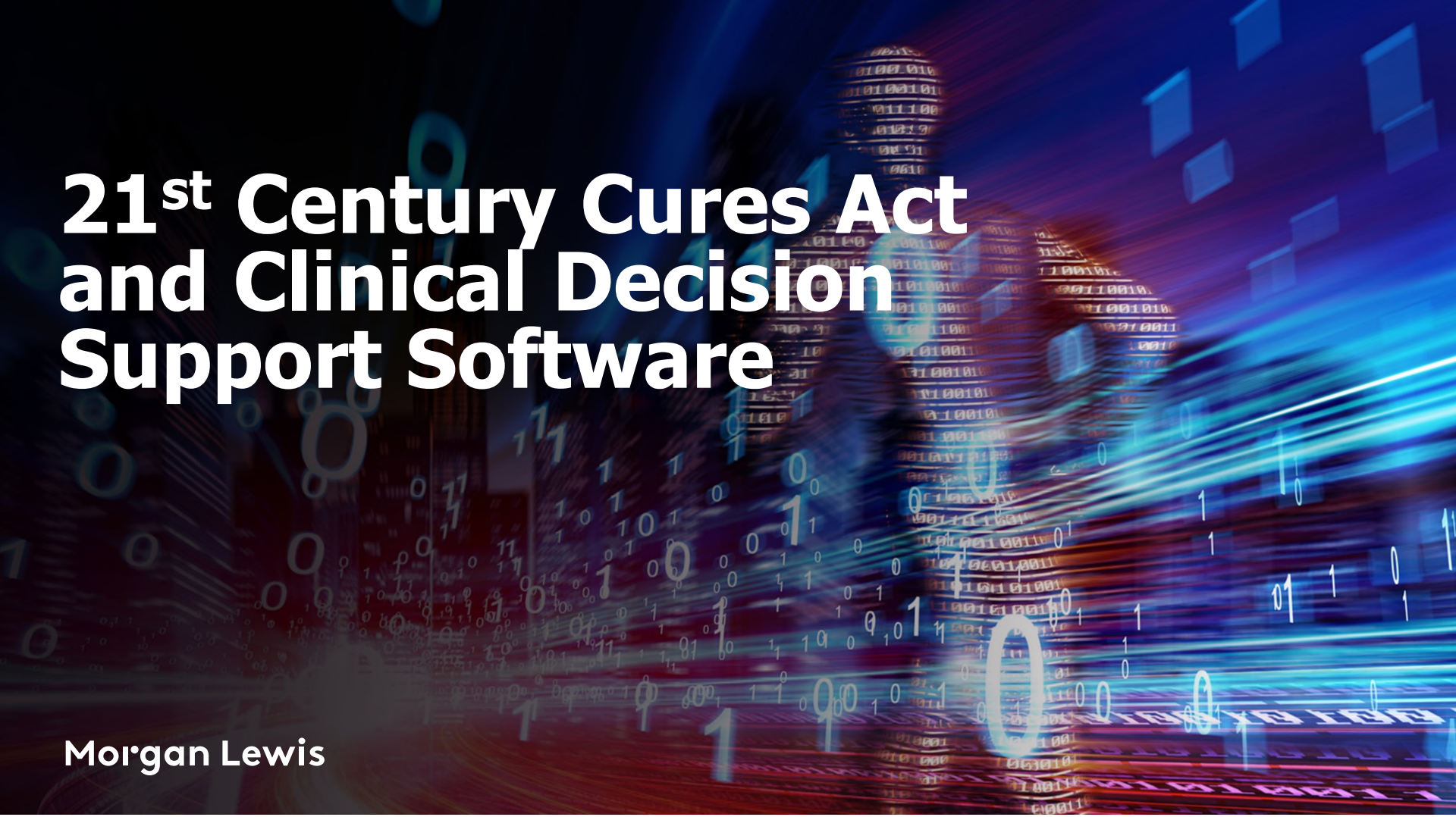
Michele L. Buenafe

Dennis C. Gucciardo

Morgan Lewis

Agenda

- 21st Century Cures Act and Clinical Decision Support Software
- AI/ML Related Developments
- Software Precertification Program
- Cybersecurity Updates
- COVID-19 Updates and Other Guidance Updates



21st Century Cures Act and Clinical Decision Support Software

Morgan Lewis

21st Century Cures Act – Software Carve Outs

- 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
- 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"
  - FDA Guidance – Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices

21st Century Cures Act – Software Carve Outs

- Medical software exemptions:
  - For *clinical decision support* (CDS) functions that meet the following criteria:
    - Is not "intended to acquire, process, or analyze a medical image or a signal from an *in vitro* diagnostic device or signal acquisition system"
    - 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)"
    - 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"
    - 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

Final Guidance issued Sept. 28, 2022

21st Century Cures Act - Report on Non-Device Software Functions

- December 2022 Report on Risks and Benefits to Health of Non-device Software Functions
  - Required under Section 3060(b) of the 21st Century Cures Act
  - Covers five categories non-device software functions per Section 520(o)(1) of the FFDCA, including software functions intended for:
    - Administrative support of a health care facility
    - Maintaining or encouraging a healthy lifestyle and unrelated to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition
    - Serving as electronic patient records when not intended to interpret or analyze patient records
    - Transferring, storing, converting formats, or displaying data
    - Providing certain types of clinical decision support to a health care provider
  - Covers time period from July 31, 2020 through July 31, 2022
  - Last report issued in November 2020

21st Century Cures Act - Report on Non-Device Software Functions

- Report requirements per Section 3060(b) of the 21st Century Cures Act
  - Timing – Not later than 2 years after enactment of the 21st Century Cures Act and every 2 years thereafter
  - Input – Must include "input from outside experts, such as representatives of patients, consumers, health care providers, startup companies, health plans or other third-party payers, venture capital investors, information technology vendors, health information technology vendors, small businesses, purchasers, employers, and other stakeholders with relevant expertise, as determined by the Secretary"
  - Substantive Focus
    - Evaluation of any risks and benefits to health associated with the non-device software functions described in Section 520(o)(1) of the FFDCA
    - Findings regarding the impact on patient safety of such non-device software functions, including best practices to promote safety, education, and competency related to such software functions

21st Century Cures Act - Report on Non-Device Software Functions

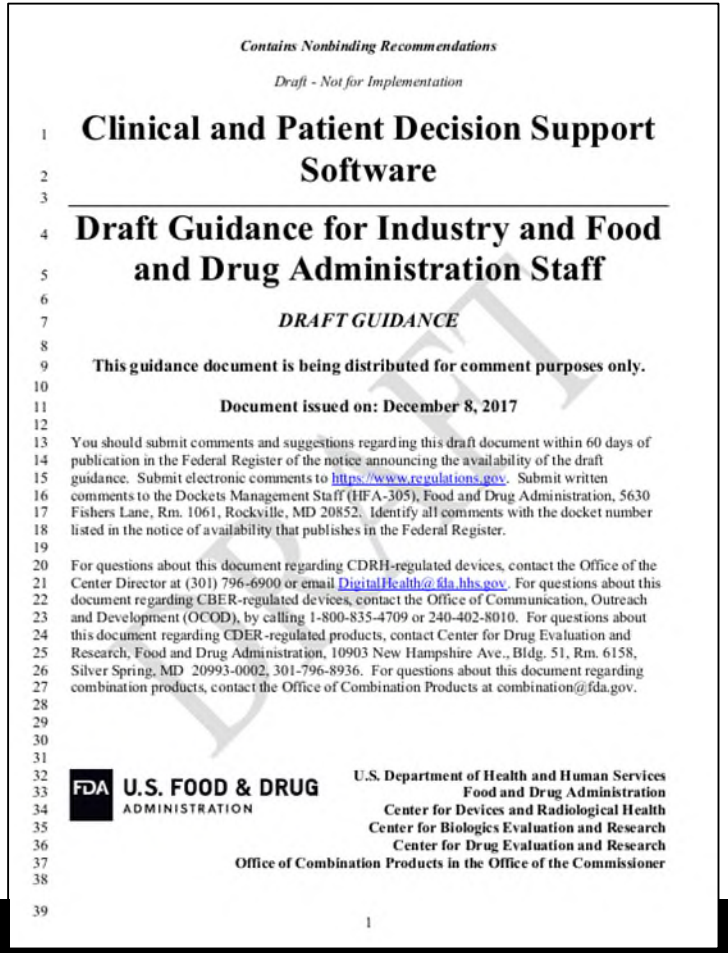
- Report findings
  - Overall, FDA found "more benefits than risks to patient safety and health related to these software functions"
  - Identified only a few reported negative impacts on patient safety and health
  - Best practice examples:
    - Software for maintaining/encouraging a healthy lifestyle
      - Recommendation to ensure that mHealth apps were evaluated to "determine whether they are beneficial to patients and whether they provide evidence-based information"
      - Observed that apps recommended by providers had greater uptake vs those that were highly rated on app marketplaces
      - Observed that "there is a general lack of standards around how these apps should be developed and brough to market"
      - Observed there is also "a lack of oversight from the companies that host these apps in their marketplace to assess if the apps are safe or beneficial to patients"
      - Recommendation for app developers to "utilize professional interface designers who understand app best practices, human behavior, and cognitive psychology in order to promote safe and effective use of the apps"

21st Century Cures Act - Report on Non-Device Software Functions

- Best practice examples:
  - Electronic patient records
    - Recommendations to ensure interoperability between EHRs and "administrative systems, patient applications, and other compiled data sources to maximize patient benefit and minimize patient risk"
    - Also noted that interoperability must have "strong privacy protections to safeguard patient data at a time when digital data sources have become more prevalent across all health care settings"
  - Clinical decision support software
    - Recommendation for CDS software developers to "address safety-related concerns and best practices in the prioritization, development, and authoring phases as well as the design, deployment, and implementation phases"
    - Ensure that CDS software uses the most "up-to-date, evidence-based information to inform recommendations" and software content is "regularly reviewed for quality and updated as needed to align with new evidence"
    - Ensure CDS software algorithms "are continuously monitored and evaluated to confirm they produce appropriate and accurate recommendations to support providers and enhance patient care"

History – 2017 Draft Guidance

- FDA issued first draft CDS Guidance in Dec. 2017
  - Intended to provide guidance on FDA's interpretation of the four statutory criteria
  - Proposed a *policy of enforcement discretion* for "Patient Decision Support Software"
  - Received significant scrutiny by industry and other stakeholders



Contains Nonbinding Recommendations

Draft - Not for Implementation

Clinical and Patient Decision Support Software

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Document issued on: December 8, 2017

You should submit comments and suggestions regarding this draft document within 60 days of publication in the Federal Register of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the Federal Register.

For questions about this document regarding CDRH-regulated devices, contact the Office of the Center Director at (301) 796-6900 or email DigitalHealth@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach and Development (OCOD), by calling 1-800-835-4709 or 240-402-8010. For questions about this document regarding CDER-regulated products, contact Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6158, Silver Spring, MD 20993-0002, 301-796-8936. For questions about this document regarding combination products, contact the Office of Combination Products at combination@fda.gov.

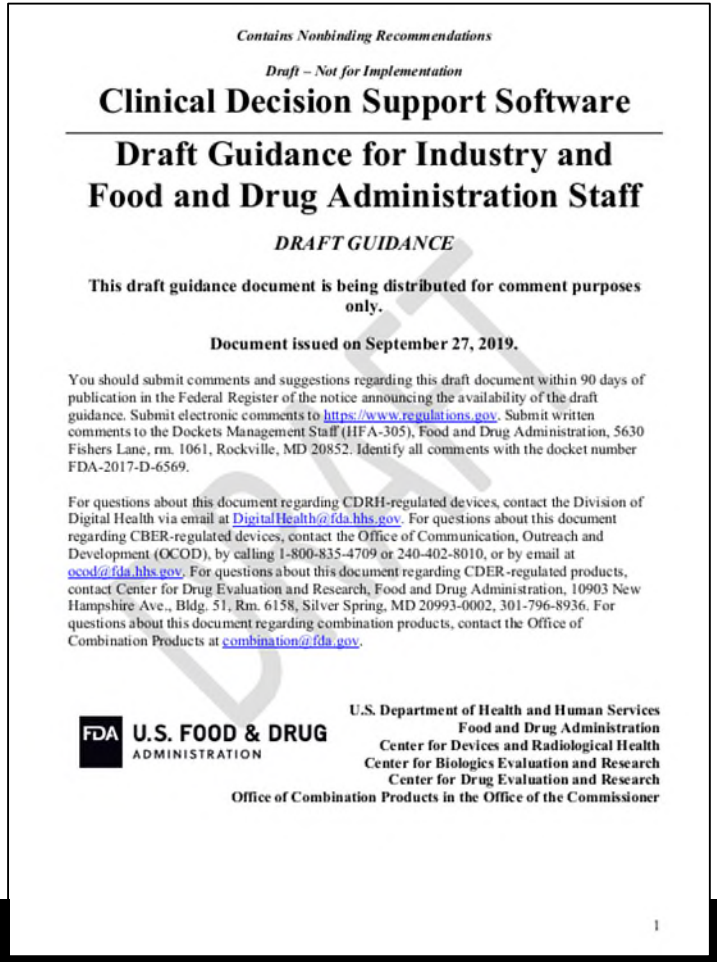
FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Office of Combination Products in the Office of the Commissioner

1

History – 2019 Draft Guidance

- Second draft guidance issued in September 2019
  - New draft guidance divided CDS software into two categories
    - Non-Device CDS
    - Device CDS
  - Proposed *policies of enforcement discretion* based on International Medical Device Regulators Forum (IMDRF) risk categorization framework
  - More lenient than the 2017 draft, but also more complex



Contains Nonbinding Recommendations

Draft – Not for Implementation

Clinical Decision Support Software

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on September 27, 2019.

You should submit comments and suggestions regarding this draft document within 90 days of publication in the Federal Register of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Identify all comments with the docket number FDA-2017-D-6569.

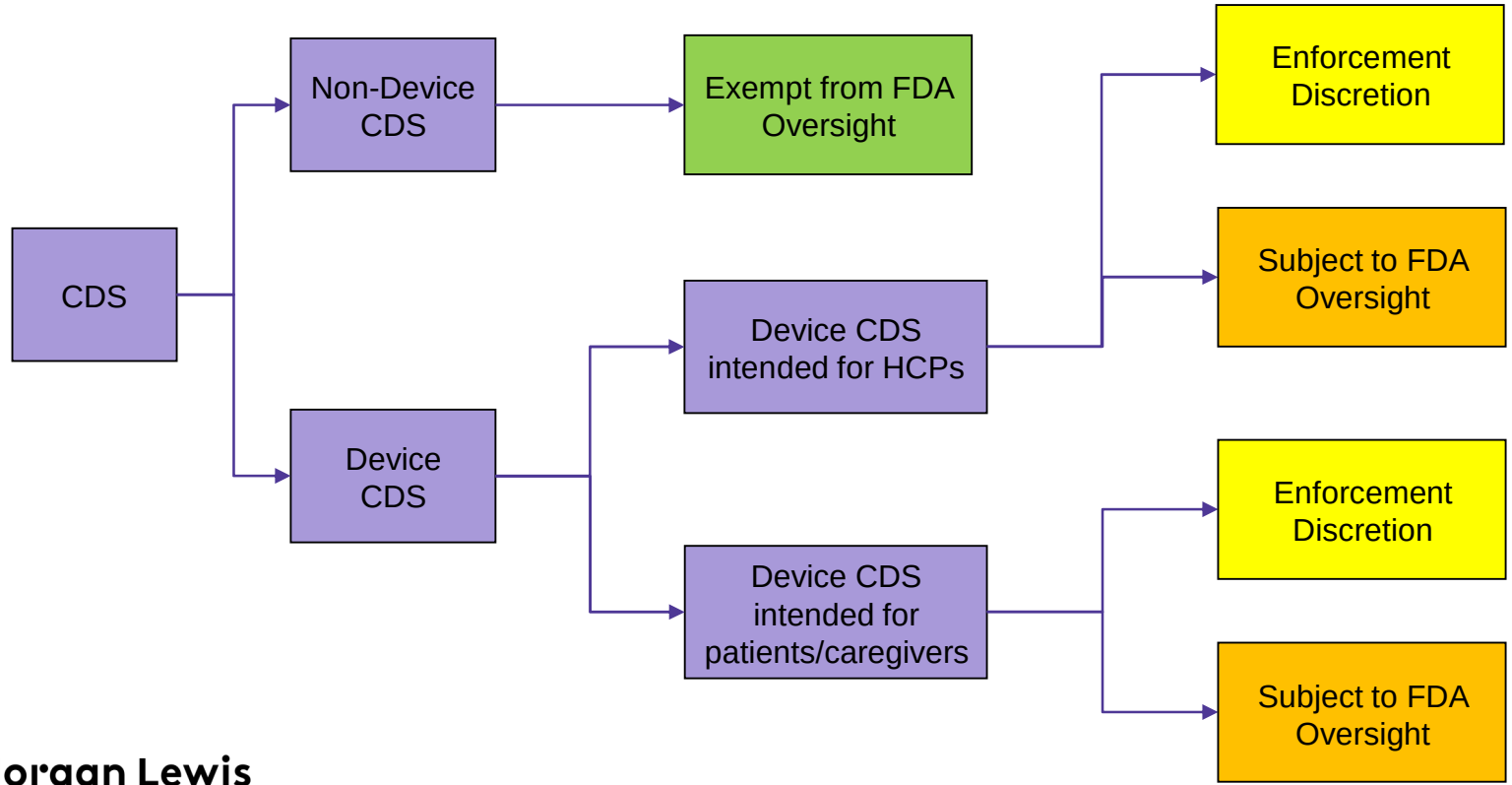
For questions about this document regarding CDRH-regulated devices, contact the Division of Digital Health via email at DigitalHealth@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach and Development (OCOD), by calling 1-800-835-4709 or 240-402-8010, or by email at ocod@fda.hhs.gov. For questions about this document regarding CDER-regulated products, contact Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6158, Silver Spring, MD 20993-0002, 301-796-8936. For questions about this document regarding combination products, contact the Office of Combination Products at combination@fda.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Office of Combination Products in the Office of the Commissioner

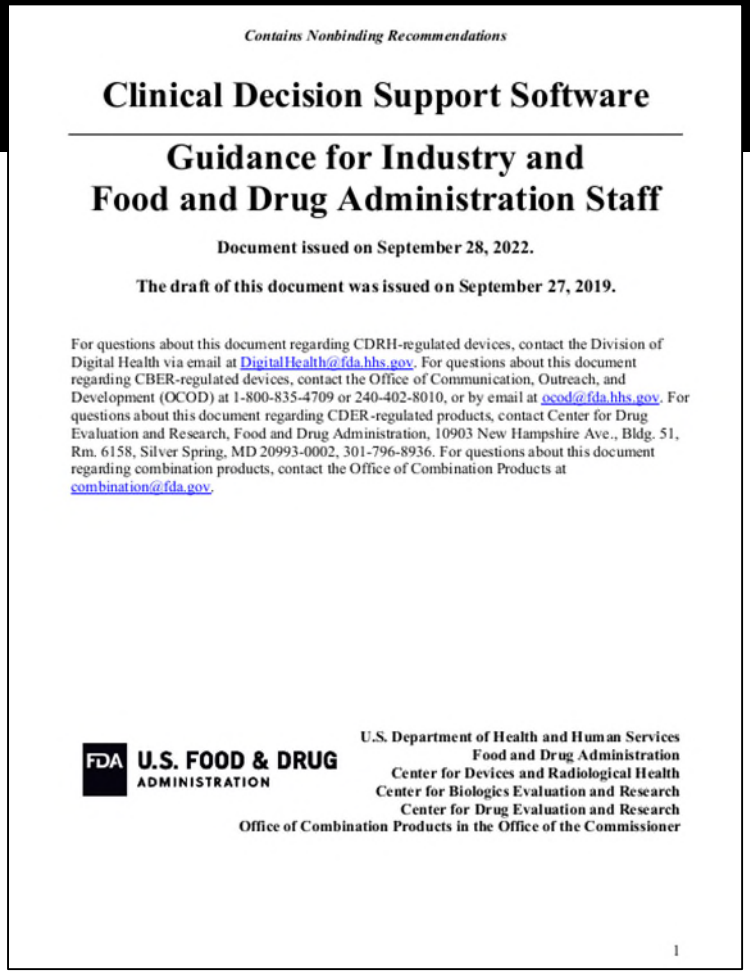
1

History – 2019 Draft Guidance



2022 Final Guidance

- Describes FDA's current interpretation of the four statutory criteria
- Simpler and more restrictive that the 2019 draft guidance
- No policies of enforcement discretion



Contains Nonbinding Recommendations

Clinical Decision Support Software

Guidance for Industry and Food and Drug Administration Staff

Document issued on September 28, 2022.

The draft of this document was issued on September 27, 2019.

For questions about this document regarding CDRH-regulated devices, contact the Division of Digital Health via email at DigitalHealth@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010, or by email at ocod@fda.hhs.gov. For questions about this document regarding CDER-regulated products, contact Center for Drug Evaluation and Research, Food and Drug Administration, 10903 New Hampshire Ave., Bldg. 51, Rm. 6158, Silver Spring, MD 20993-0002, 301-796-8936. For questions about this document regarding combination products, contact the Office of Combination Products at combination@fda.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Office of Combination Products in the Office of the Commissioner

1

2022 Final Guidance – Criterion 1

- Criterion 1 – software function is not "intended to acquire, process, or analyze a medical image or a signal from an *in vitro* diagnostic device or signal acquisition system"
- New guidance state that "FDA considers software functions that *assess or interpret* the clinical implications or clinical relevance of a *signal, pattern, or medical image* to be software functions that *do not meet Criterion 1*"
  - The term *signal* to includes signals that "typically require the use of" an IVD or signal acquisition system
    - A *signal acquisition system* includes devices that "measure a parameter from within, attached to, or external to the body for a medical purpose," which may include use of sensors, collection of samples or specimens, or use of radiological imaging
  - The term *medical image* includes both images generated by use of medical imaging systems and also images that, although not originally acquired for a medical purpose, are processed or analyzed for a medical purpose
  - The term *pattern* is defined to include "multiple, sequential, or repeated measurements of a signal or from a signal acquisition system"

2022 Final Guidance – Criterion 2

- Criterion 2 – the software function 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)"
  - The term *medical information about a patient* is restricted to information where "the relevance of the information to the clinical decision being made is well understood and accepted" in the practice of medicine, such as test results, symptoms, demographic information, certain medical device outputs (e.g., heart rate or blood pressure readings), and patient discharge summaries
  - The term *other medical information* is restricted to include information "such as peer-reviewed clinical studies, clinical practice guidelines, and information that is similarly independently verified and validated as accurate, reliable, not omitting information, and supported by evidence
- The final guidance requires that medical information be used as an input for the CDS software, which may include a "single, discreet test or measurement result that is clinically meaningful," while "more continuous sampling of the same information [...] is a pattern/signal" per Criterion 1
  - Thus, FDA reads into the statute a restriction related to "sampling frequency" for Criterion 2

2022 Final Guidance – Criterion 3

- Criterion 3 – the software function 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"
- FDA takes a more restrictive approach to this criterion by limiting scope to include software that generates recommendations intended to "enhance, inform, and/or influence a health care decision" but not intended to "replace or direct the HCP's judgement"
- This *excludes* any software used "in time-critical decision making and in cases where a software function provides a specific preventive, diagnostic, or treatment output or directive"
  - This new exclusion appears to add new restrictions to the language "provides recommendations" from the statute, as anything approaching a definitive recommendation would fall under this new exclusion
  - This includes, for example, software that provides "a specific preventative, diagnostic, or treatment course", indicates "that a specific patient 'may exhibit signs' of a disease or condition", or "identifies a risk probability or risk score for a specific disease or condition

2022 Final Guidance – Criterion 4

- Criterion 4 – software function 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 final guidance returns to its original 2017 approach to impose new restrictions for CDS software for the purpose of "enabling the HCP to independently review the basis of the recommendations" the software presents
- Provides several labeling recommendations, including:
  - The software or software labeling should include the intended use of the product, which cannot be time critical, the intended HCP user, and the intended patient population
  - The software or software labeling should "identify the required input medical information, with plain language instructions on how the inputs should be obtained, their relevance, and data quality requirements"
  - The software or software labeling should provide a "plain language description of the underlying algorithm development and validation that forms the basis for the CDS implementations"
    - This includes: a summary of the logic or methods relied upon (e.g., statistical modeling or AI/ML techniques), a description of the data relied upon, and a description of clinical validation study results
  - The software output should provide the HCP with "relevant patient-specific information and other knowns/unknowns for consideration (e.g., missing, corrupted, or unexpected input data values)" that will allow the HCP to independently review the CDS recommendations and apply their judgment

Examples – Software that Qualifies as CDS

- Providing evidence-based clinician order sets for an HCP to choose from, tailored for a particular condition, disease, or clinician preference
- Matching patient-specific medical information from records or reports to reference information (e.g., clinical guidelines) that is routinely used in clinical practice
- Drug-drug interaction and drug-allergy contraindication notifications to avert adverse drug reaction
- Prioritized list of preventive, diagnostic or treatment options

Examples – Software that does NOT Qualify as CDS

- Software function that uses a patient's image sets (e.g., CT, magnetic resonance (MR)) to create an individual treatment plan for review by an HCP for patients undergoing radiation therapy treatment with external beam or brachytherapy
- Software function that identifies patients with possible diagnosis of opioid addiction based on analysis of patient-specific medical information, family history, prescription patterns, and geographical data
- Software function that analyzes multiple signals (e.g., perspiration rate, heart rate, eye movement, breathing rate) from wearable products to monitor whether a person is having a heart attack or narcolepsy episode
- Software function that analyzes patient-specific medical information to detect a life-threatening condition, such as stroke or sepsis, and generate an alarm or an alert to notify an HCP
- Software function that analyzes sound waves captured when users cough or recite certain sentences to diagnose bronchitis or sinus infection
- Software function that provides a prioritized list of FDA-authorized depression treatment options to an HCP based on an analysis of reported outcomes in a database of clinical studies using medical information (e.g., diagnosis and demographics) from the patient's medical record

Examples – Analyzing Test Results

- Software that analyzes test results appears to be excluded under Criterion 1
- However, certain examples of in the final guidance of software that qualifies as CDS permit analysis of test results:
  - Software function that flags patient results for an HCP based on specific clinical parameters (e.g., out of range test results where the reference ranges are predetermined by the lab or HCP) in response to a medication order
  - Software function that analyzes blood glucose laboratory test results and pre-diabetes diagnosis from a patient's medical record and provides an HCP with a list of next-step options to consider, such as more frequent office visits or referral to a specialist
  - Software function that analyzes patient-specific medical information (e.g., end stage renal disease (ESRD) diagnosis, lab test results, and patient demographics from the patient's medical record) and provides an HCP with a list of treatment options for ESRD based on implementation of practice guidelines

AI/ML Related Developments

Morgan Lewis

Artificial Intelligence/Machine Learning Software

- Impact of final CDS Software Guidance
  - Prior 2019 draft guidance included language suggesting certain ML software could either qualify as CDS software or qualify for enforcement discretion
    - ML software could qualify as CDS software if the HCP-user could evaluate the basis of the software's recommendations because the logic and inputs of the ML algorithm were explained and available to the HC
    - ML software could qualify for enforcement discretion if the software only provides clinical information for non-serious situations or conditions
  - New final guidance does include any examples on AI/ML software and appears to exclude such software from the scope of CDS exemption

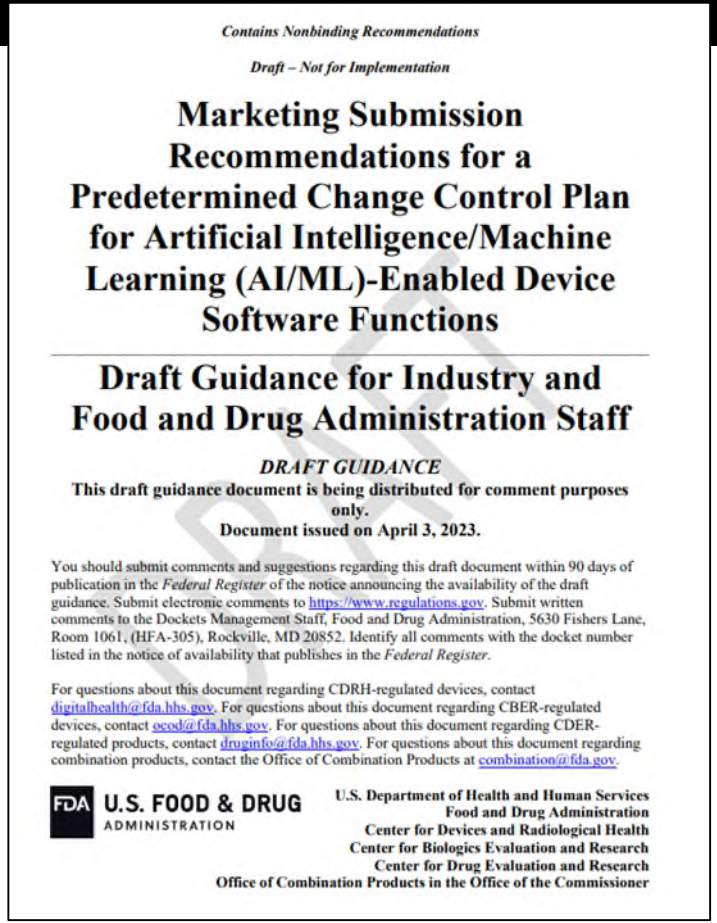
Artificial Intelligence/Machine Learning Software

- April 2019 Discussion Paper - Proposed framework to address how FDA would handle postmarket modifications to AI/ML software devices
  - Existing model 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 control risks for the permitted changes and how the changes may occur

Artificial Intelligence/Machine Learning Software

- New Draft Guidance for Predetermined Change Control Plans (PCCPs) for ML-enable device software functions, to include:

1. A detailed description of the specific, planned device modifications
2. The associated methodology to develop, validate, and implement the modifications in a manner to ensure continued safety and effectiveness
3. An Impact Assessment to describe the assessment of the benefits and risks of the planned modifications and risk mitigations



Contains Nonbinding Recommendations

Draft – Not for Implementation

Marketing Submission Recommendations for a Predetermined Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on April 3, 2023.

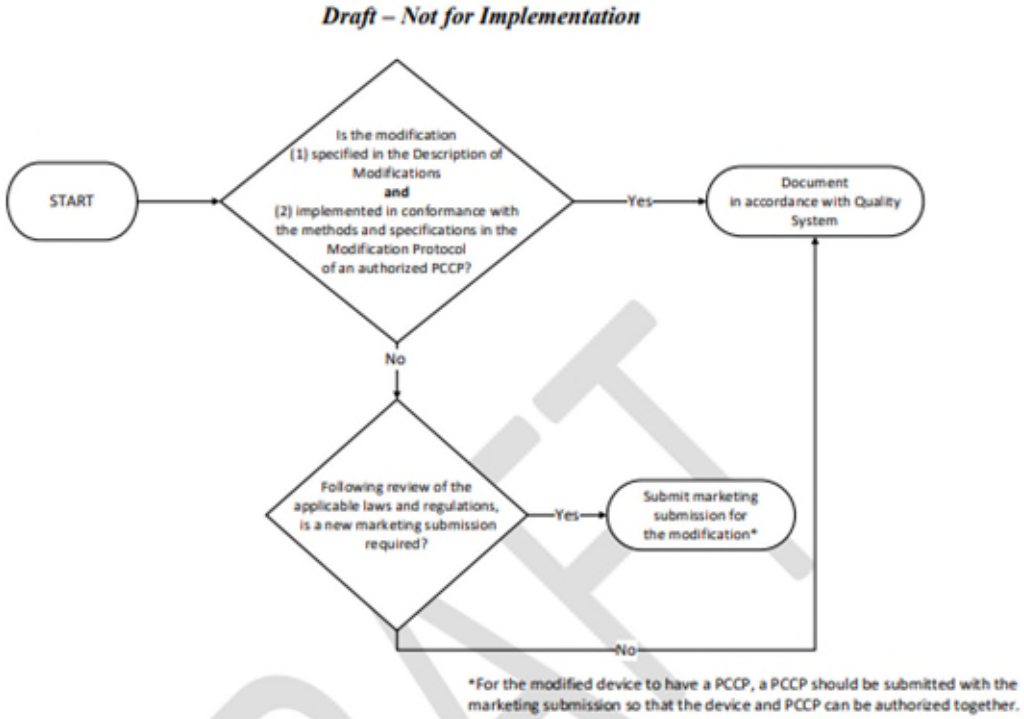
You should submit comments and suggestions regarding this draft document within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document regarding CDRH-regulated devices, contact digitalhealth@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact ocod@fda.hhs.gov. For questions about this document regarding CDER-regulated products, contact druginfo@fda.hhs.gov. For questions about this document regarding combination products, contact the Office of Combination Products at combination@fda.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research
Center for Drug Evaluation and Research
Office of Combination Products in the Office of the Commissioner

Artificial Intelligence/Machine Learning Software

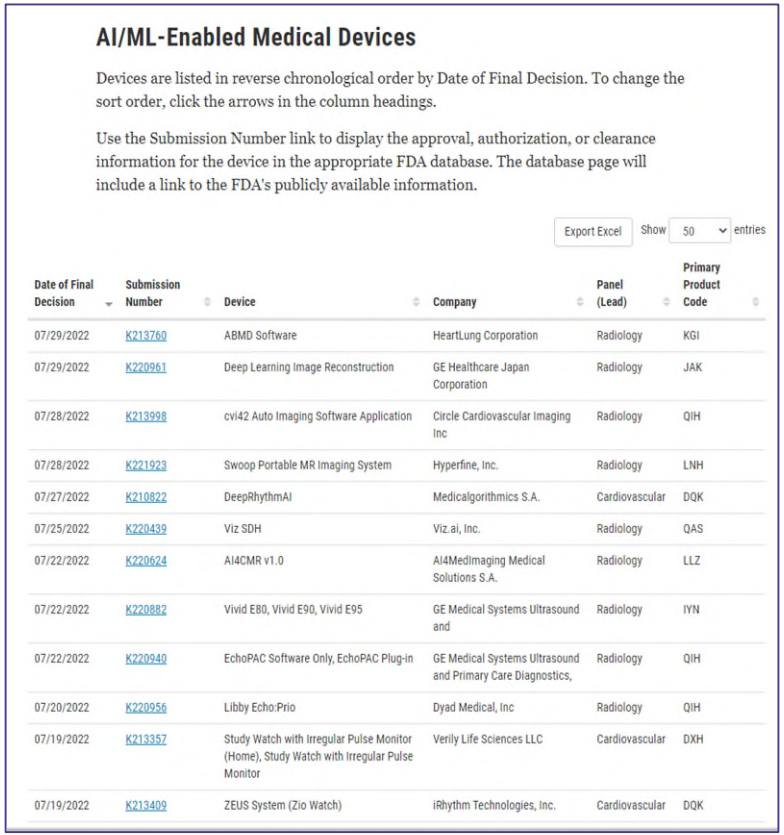


- Modifications consistent with the authorized PCCP would not require a new premarket submission
- Modifications outside the scope of the PCCP would need to be assessed per existing laws and regulations
- Modification of the PCCP itself generally would require a new premarket submission

AI/ML-Enabled Medical Devices

- Current FDA list includes over 500 devices from 1995 through July 2022
  - Vast majority cleared via 510(k) process
  - 18 *de novo* submissions
  - 3 premarket approval applications (PMAs)

- Review Branch
  - Significant majority in Radiology, followed by Cardiovascular, Hematology, and Neurology



AI/ML-Enabled Medical Devices

Devices are listed in reverse chronological order by Date of Final Decision. To change the sort order, click the arrows in the column headings.

Use the Submission Number link to display the approval, authorization, or clearance information for the device in the appropriate FDA database. The database page will include a link to the FDA's publicly available information.

Export Excel Show 50 entries

Date of Final Decision	Submission Number	Device	Company	Panel (Lead)	Primary Product Code
07/29/2022	K213760	ABMD Software	HeartLung Corporation	Radiology	KGI
07/29/2022	K220961	Deep Learning Image Reconstruction	GE Healthcare Japan Corporation	Radiology	JAK
07/28/2022	K213998	cvi42 Auto Imaging Software Application	Circle Cardiovascular Imaging Inc	Radiology	QIH
07/28/2022	K221923	Swoop Portable MR Imaging System	Hyperfine, Inc.	Radiology	LNH
07/27/2022	K210822	DeepRhythmAI	MedicalgorithmIcs S.A.	Cardiovascular	DQK
07/25/2022	K220439	Viz SDH	Viz.ai, Inc.	Radiology	QAS
07/22/2022	K220624	AI4CMR v1.0	AI4MedImaging Medical Solutions S.A.	Radiology	LLZ
07/22/2022	K220882	Vivid E80, Vivid E90, Vivid E95	GE Medical Systems Ultrasound and	Radiology	IYN
07/22/2022	K220940	EchoPAC Software Only, EchoPAC Plug-in	GE Medical Systems Ultrasound and Primary Care Diagnostics,	Radiology	QIH
07/20/2022	K220956	Libby Echo:Prio	Dyad Medical, Inc	Radiology	QIH
07/19/2022	K213357	Study Watch with Irregular Pulse Monitor (Home), Study Watch with Irregular Pulse Monitor	Verily Life Sciences LLC	Cardiovascular	DXH
07/19/2022	K213409	ZEUS System (Zio Watch)	iRhythm Technologies, Inc.	Cardiovascular	DQK

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

Commitment	"Action"
1. Further develop the proposed regulatory framework	Draft guidance document issued in 2023 that will discuss the use of predetermined change control plans (for software learning over time)
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 • Discussion paper issued October 2021
3. Foster a patient-centered approach, including device transparency to users	Hold a public workshop in Oct. 2020 to share learnings and to elicit input from the broader community on how device labeling supports transparency to users
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
5. Advance real-world performance (RWP) monitoring pilots	Work with stakeholders on a voluntary basis to support RWP monitoring pilots

Good Machine Learning Practice for Medical Device Development: Guiding Principles

10 "Guiding Principles" developed jointly by FDA, Health Canada, and MHRA

1. Multi-Disciplinary Expertise Is Leveraged Throughout the Total Product Life Cycle
2. Good Software Engineering and Security Practices Are Implemented
3. Clinical Study Participants and Data Sets Are Representative of the Intended Patient Population
4. Training Data Sets Are Independent of Test Sets
5. Selected Reference Datasets Are Based Upon Best Available Methods
6. Model Design Is Tailored to the Available Data and Reflects the Intended Use of the Device
7. Focus Is Placed on the Performance of the Human-AI Team
8. Testing Demonstrates Device Performance during Clinically Relevant Conditions
9. Users Are Provided Clear, Essential Information
10. Deployed Models Are Monitored for Performance and Re-training Risks are Managed

Software Precertification Program

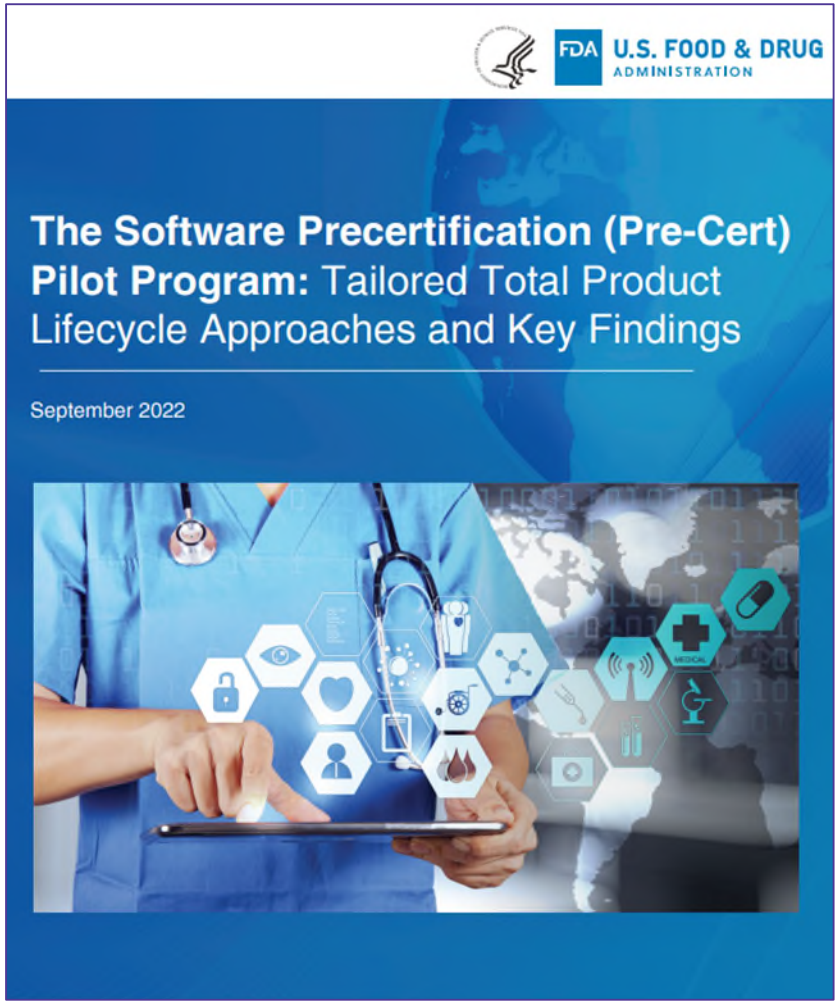
Morgan Lewis

Software Pre-Certification Program – History

- July 2017: Announced a voluntary pilot program for digital health developers
  - Intended to help FDA gather information and experience in order to create a pre-certification program
- 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
- January 2019: FDA issues three new documents:
  - Version 1.0 of the Working Model
  - 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
  - Regulatory Framework for Conducting the Pilot Program
- September 2020: Update on Progress of Pre-Cert Pilot Program
  - 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."

Software Pre-Certification Program

- Key findings from Working Model and Pilot:
  - "FDA has found that rapidly evolving technologies in the modern medical device landscape could benefit from a new regulatory paradigm, which would require a legislative change"
  - "Given the challenges faced during the pilot, FDA has determined that the approach described in the Working Model is not practical to implement under our current statutory and regulatory authorities. However, the pilot informed what new statutory authorities could support a future regulatory paradigm that builds on these concepts."




Cybersecurity
Updates
Morgan Lewis

Cybersecurity Threats and Medical Devices

How many people have been affect
WannaCry?

Over the weekend, Europol officials said
computers have been hit by the malware.
certainly risen as people in Asia — who had logged off for the workweek before WannaCry began spreading — have returned to work. On Monday, the Japanese electronics maker Hitachi, a prominent Korean theater chain and the Chinese government said their systems had been affected. Chinese state media reported that 40,000 businesses and institutions have been hit, according to NPR, including universities, gas stations and city services.

And that's just a measure of the electronic consequences of WannaCry. The software attack has taken a toll on many people in the real world. Health care providers in Britain's NHS, for example, were forced to turn ambulances away and cancel or delay cancer treatments for patients over the weekend, though officials say 80 percent of the NHS's systems were unaffected and that the disruption is easing.

LILY HAY NEWMAN SECURITY AUG 9, 2018 12:30 PM

A New Pacemaker Hack Puts Malware Directly on the Device

Researchers at the Black Hat security conference will demonstrate a new pacemaker-hacking technique that can add or withhold shocks at will.

Unpatched and Outdated Medical Devices Provide Cyber Attack Opportunities

Summary

The FBI has identified an increasing number of vulnerabilities posed by unpatched medical devices that run on outdated software and devices that lack adequate security features. Cyber threat actors exploiting medical device vulnerabilities adversely impact healthcare facilities' operational functions, patient safety, data confidentiality, and data integrity. Medical device vulnerabilities predominantly stem from device hardware design and device software management. Routine challenges include the use of standardized configurations, specialized configurations, including a substantial number of managed devices on the network, lack of device embedded security features, and the inability to upgrade those features.

FDA’s Cybersecurity Journey

- October 2014: Final Guidance, Content of Premarket Submission for Management of Cybersecurity in Medical Devices
- October 2018: Draft Guidance, Premarket Submissions for Management of Cybersecurity in Medical Devices
- April 2022: Draft Guidance, Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions
- December 2022: Section 3305 of the Omnibus -- "Ensuring Cybersecurity of Medical Devices‟ (enacted March 29, 2023)

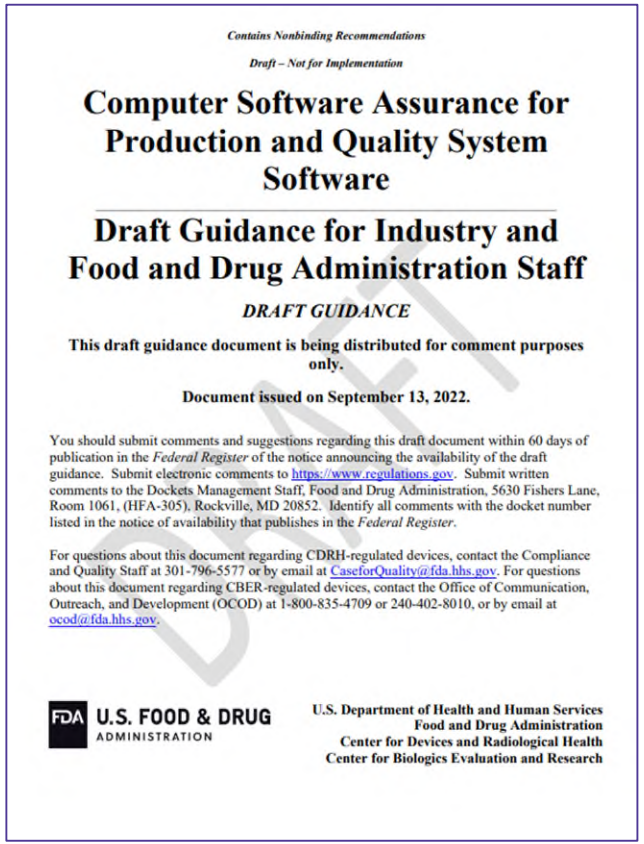
April 2022: Draft Guidance, Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions

- Cybersecurity as part of QSR requirements
- Software Bill of Materials (SBOM)
- Risk Management and use of "Threat Modeling"
- Use of a Secure Product Development Framework
- Transparency
  - Labeling Recommendations
  - Vulnerability Management Plans

Food and Drug Omnibus Reform Act (FDORA)

- Imposes new requirements for "cyber devices", defined to include any device that:
  "(A) includes software, including software as or in a device;
  "(B) has the ability to connect to the internet; or
  " (C) contains any such technological characteristics that could be vulnerable to cybersecurity threats
- Requires manufacturers/developers of cyber devices to meet certain cybersecurity requirements
- Requires a cyber device applicant to include in its premarket submissions such information as FDA may require to ensure the cyber device meets cybersecurity requirements
- Allows FDA to issue an NSE finding for a 510(k) covering a cyber device based on FDA's finding that the cybersecurity information on the 510(k) is inadequate for the device in its use environment
  - Submissions post October 1, 2023 must comply with requirements of act
- Makes failure to comply with the cybersecurity requirements a prohibited act

Computer Software Assurance for Production and Quality System Software – Final Guidance



Contains Nonbinding Recommendations

Draft – Not for Implementation

Computer Software Assurance for Production and Quality System Software

Draft Guidance for Industry and Food and Drug Administration Staff

DRAFT GUIDANCE

This draft guidance document is being distributed for comment purposes only.

Document issued on September 13, 2022.

You should submit comments and suggestions regarding this draft document within 60 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff, Food and Drug Administration, 5630 Fishers Lane, Room 1061, (HFA-305), Rockville, MD 20852. Identify all comments with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions about this document regarding CDRH-regulated devices, contact the Compliance and Quality Staff at 301-796-5577 or by email at CaseforQuality@fda.hhs.gov. For questions about this document regarding CBER-regulated devices, contact the Office of Communication, Outreach, and Development (OCOD) at 1-800-835-4709 or 240-402-8010, or by email at ocod@fda.hhs.gov.

FDA U.S. FOOD & DRUG ADMINISTRATION

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health
Center for Biologics Evaluation and Research

- New draft guidance provides recommendations for "computer software assurance" for software and automated systems used for medical device production or quality
- Describe various methods and testing activities to establish "computer software assurance" and ensure compliance with QSR (including software validation) and other regulatory requirements.

COVID-19 and Other Guidance Updates

Morgan Lewis

Other Guidance Documents

- FDA updated other guidance documents to align with new CDS Software Guidance
  - Policy for Device Software Functions and Mobile Medical Applications
  - Changes to Existing Medical Software Policies Resulting from Section 3060 of the 21st Century Cures Act
- Other recent FDA guidance impacting digital health software
  - Computer Software Assurance for Production and Quality System Software – Draft Guidance (Sept. 28, 2022)
  - Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions – Draft Guidance (Dec. 23, 2021)
  - Digital Health Technologies for Remote Data Acquisition in Clinical Investigations – Draft Guidance (Dec. 21, 2022)

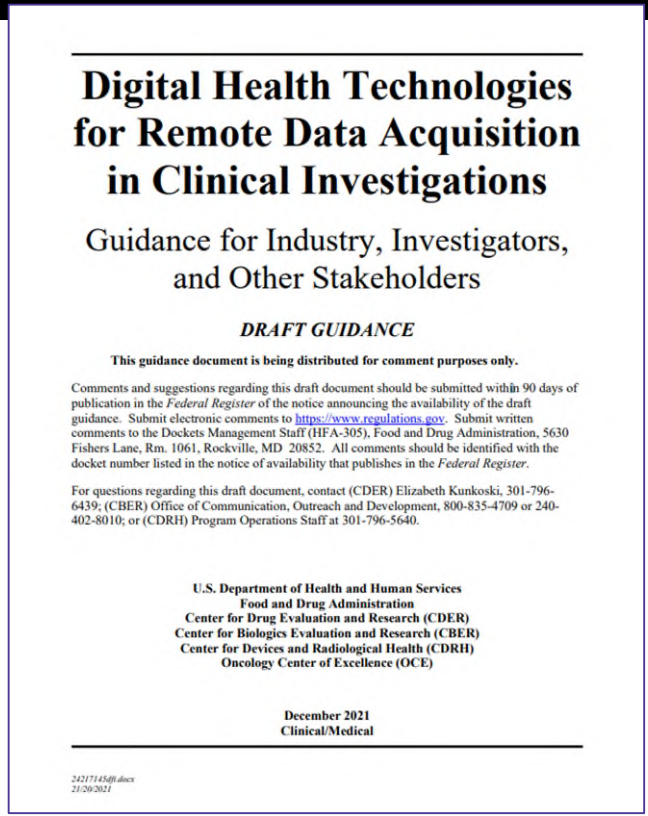
Assessing the Credibility of Computational Modeling and Simulation in Medical Device Submissions

- Sets forth a proposed 9-step process to assess the credibility of computational modeling and simulation (CM&S) used to support a medical device premarket submission

1. Describe the question(s) of interest to be addressed
2. Define the context of use (COU) of the computational model
3. Determine the model risk
4. Identify and categorize the credibility evidence
5. Define credibility factors for the proposed credibility evidence and set prospective credibility goals
6. Perform prospective adequacy assessment
7. Generate the credibility evidence by executing the proposed study(ies) and/or analyzing previously generated data
8. Determine if credibility goals were met and perform post-study adequacy assessment
9. Prepare a report on the credibility of the CM&S

Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

- Applies to ALL types of clinical investigations utilizing a digital health technology (DHT) for remote data acquisition
- A DHT defined as "a system that uses computing platforms, connectivity, software, and/or sensors, for healthcare and related uses."
- Guidance covers considerations when using DHTs in clinical investigations
  - Selection of a Digital Health Technology and Rationale for Use in a Clinical Investigation
  - Digital Health Technology Description in a Submission
  - Verification, Validation, and Usability of Digital Health Technologies
  - Evaluation of Clinical Endpoints From Data Collected Using Digital Health Technologies
  - Statistical Analysis
  - Risk Considerations When Using Digital Health Technologies
  - Record Protection and Retention
  - Other Considerations When Using Digital Health Technologies During a Clinical Investigation



Digital Health Technologies for Remote Data Acquisition in Clinical Investigations

Guidance for Industry, Investigators, and Other Stakeholders

DRAFT GUIDANCE

This guidance document is being distributed for comment purposes only.

Comments and suggestions regarding this draft document should be submitted within 90 days of publication in the *Federal Register* of the notice announcing the availability of the draft guidance. Submit electronic comments to https://www.regulations.gov. Submit written comments to the Dockets Management Staff (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. All comments should be identified with the docket number listed in the notice of availability that publishes in the *Federal Register*.

For questions regarding this draft document, contact (CDER) Elizabeth Kunkoski, 301-796-6439; (CBER) Office of Communication, Outreach and Development, 800-835-4709 or 240-402-8010; or (CDRH) Program Operations Staff at 301-796-5640.

U.S. Department of Health and Human Services
Food and Drug Administration
Center for Drug Evaluation and Research (CDER)
Center for Biologics Evaluation and Research (CBER)
Center for Devices and Radiological Health (CDRH)
Oncology Center of Excellence (OCE)

December 2021
Clinical/Medical

24217145dft.docx
21/20/2021

Guidance Document Priorities FY 2023

- A-List Priorities
  - Final Guidance, Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions
  - Final Guidance, Content of Premarket Submissions for Device Software Functions
  - Final Guidance, Transition Plan for Medical Devices That Fall Within Enforcement Policies Issued During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency
  - Final Guidance, Transition Plan for Medical Devices Issued Emergency Use Authorizations (EUAs) During the Coronavirus Disease 2019 (COVID-19) Public Health Emergency
- B-List Priorities
  - Draft Guidance, Marketing Submission Recommendations for A Change Control Plan for Artificial Intelligence/Machine Learning (AI/ML)-Enabled Device Software Functions
- Removed from Priority List:
  - Risk Categorization for Software as a Medical Device: FDA Interpretation, Policy, and Considerations

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

Transition Plan for Medical Devices That Fall Within COVID-19 Enforcement Policies

- Final guidance documents issued March 27, 2023
- 180-day transition period once PHE expires (May 11, 2023)
- Three phased transition plan:
  - Phase 1 begins May 11, 2023
    - Requires compliance with Part 803 for MDRs
  - Phase 2 begins August 9, 2023
    - Requires compliance with Part 806 (corrections/removals reporting) and Part 807 (registration/listing)
  - Phase 3 begins November 7, 2023
    - FDA withdraws the enforcement policies
    - Requires compliance with all applicable regulatory requirements (including QSR, labeling, UDI, etc.)

FDA Emergency Use Authorizations for Software

Tiger Tech COVID Plus Monitor	Symptom screening by identifying certain biomarkers, when performed following a temperature reading
COVIage	Predictive Screening to assist with the early identification of COVID-19 patients who are likely to be diagnosed with hemodynamic instability or respiratory decompensation
CLEW Medical	Predictive screening to assist with the early identification of patients who are likely to be diagnosed with respiratory failure or hemodynamic instability
Eko ELEFT	Screening for potential cardiac complications associated with COVID-19

FDA Emergency Use Authorizations for Wearables and Remote Monitoring

VSMS Patch	Remote monitoring of the QT interval of an electrocardiogram for patients in general care and those undergoing treatment for COVID-19
teleCare	Nurse call system updated with capability for remote communication between patients and healthcare providers
VitalPatch	Remote monitoring of the QT interval of an electrocardiogram for patients in general care and those undergoing treatment for COVID-19
IntelliVue Patient Monitors	Remote monitoring of adult, pediatric, and neonate patients having or suspected of having COVID-19

Transition Plan for Medical Devices Issued Emergency Use Authorizations (EUAs) Related to COVID-19

- Final guidance documents issued March 27, 2023
- Manufacturers will have 180 days to submit a marketing application (e.g., 510(k)) once HHS publishes a notice of termination of its authority provided under Section 564 of the FFDCA to issue EUAs (the "EUA Termination Date")
  - After the 180 days, a manufacturers may continue to market its device while its application is pending, *provided that* FDA accepted the application for substantive review (i.e., cleared "Refuse to Accept") prior to the end of the 180-day period
  - After the 180 days, manufacturers will need to comply with the general controls for medical device, including the QSR, MDR, and registration and listing requirements – except for device labeling and UDI
- After EUA Termination Date, COVID-19 LDTs would be treated like any other LDT (subject to LDT enforcement discretion policy)

Biography

Michele L. Buenafe
Washington, D.C.
+1.202.739.6326
michele.buenafe@morganlewis.com

Michele L. Buenafe is a partner in the FDA practice and serves as co-leader of the firm's Digital Health initiative. She advises clients on regulatory, compliance, and enforcement issues related to the development, manufacturing, marketing, labeling, and advertising of medical devices, human tissue products, pharmaceuticals, controlled substances, listed chemicals, and combination products. She also advises clients on emerging legal issues relating to digital health platforms such as mobile medical apps, clinical decision support software, telemedicine systems, wearable devices, and other health information technology.

Biography

Dennis C. Gucciardo
Washington, D.C.
+1.202.739.5278
dennis.gucciardo@morganlewis.com

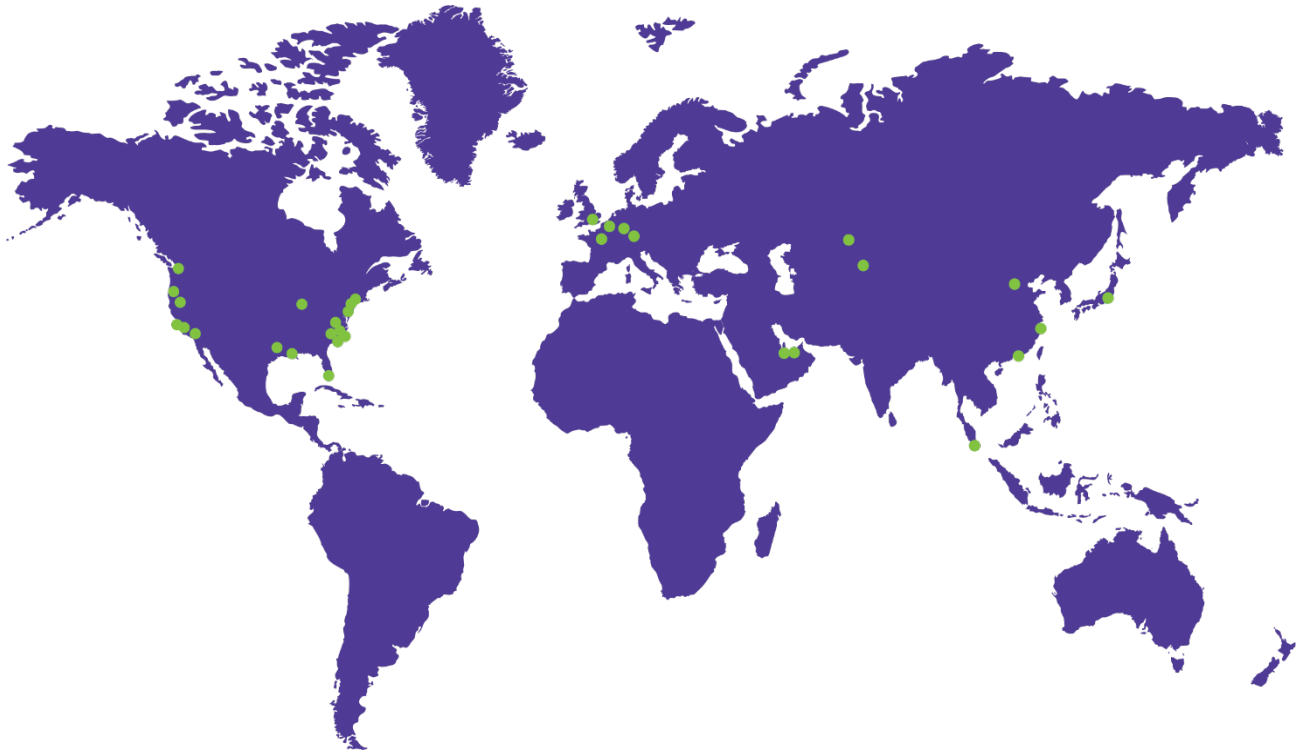
Dennis C. Gucciardo counsels domestic and global medical device manufacturers to help ensure they are operating in compliance with the myriad of US Food and Drug Administration (FDA) regulations, requirements, and expectations. He works with companies—from small startups to large multinational corporations—throughout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

Our Global Reach

Africa
Asia Pacific
Europe
Latin America
Middle East
North America

Our Locations

Abu Dhabi
Almaty
Astana
Beijing
Boston
Brussels
Century City
Chicago
Dallas
Dubai
Frankfurt
Hartford
Hong Kong
Houston
London
Los Angeles
Miami
Munich
New York
Orange County
Paris
Philadelphia
Pittsburgh
Princeton
San Francisco
Seattle
Shanghai
Silicon Valley
Singapore
Tokyo
Washington, DC
Wilmington



Morgan Lewis

THANK YOU