PROGRAM MATERIALS
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New Set of Guidance from FDA Provides Clarity on Digital Health Policies, Clinical Decision Support

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FDA Guidance on Digital Health Policies, Clinical Decision Support (CDS)

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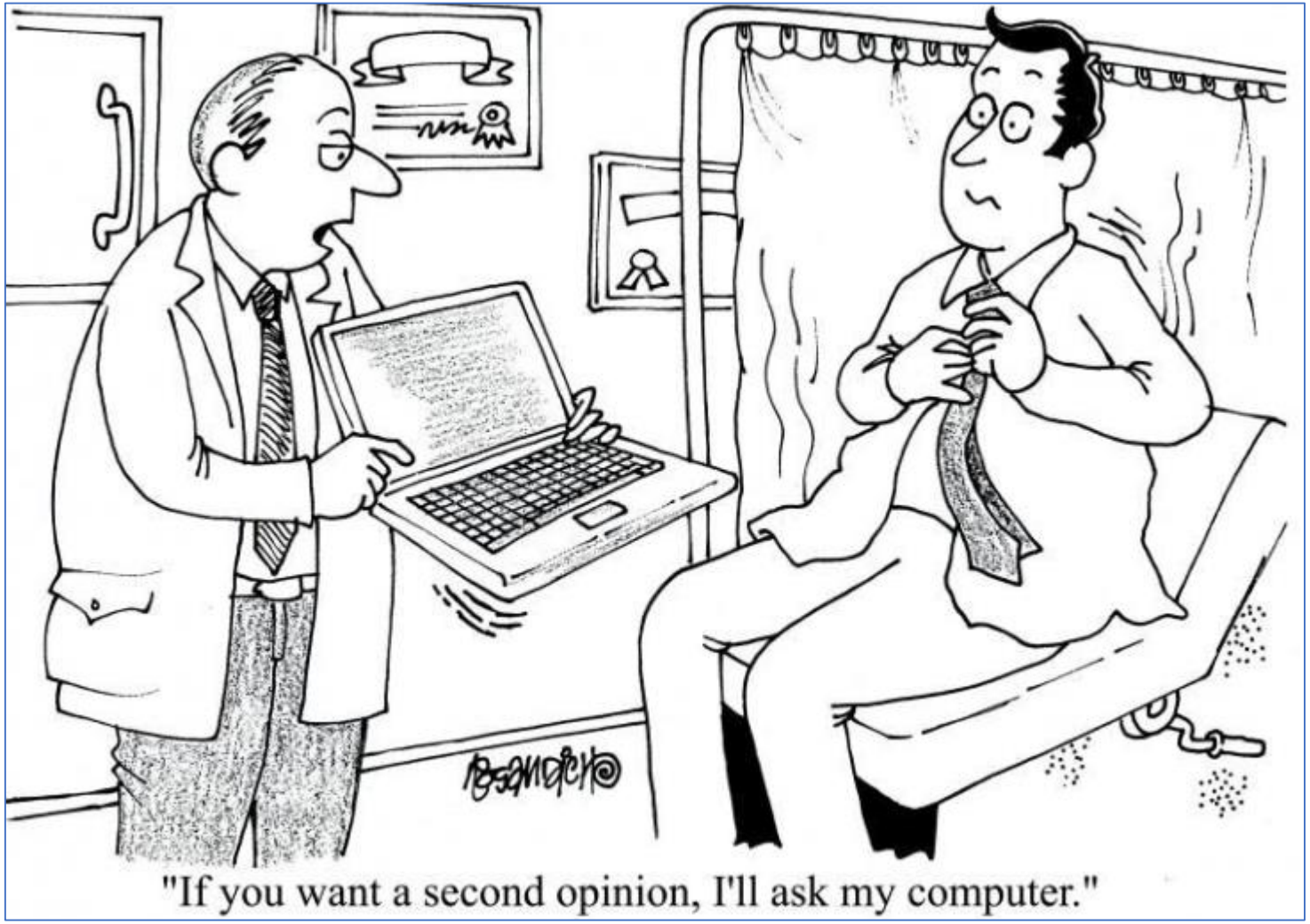
Agenda

- The Basics of Clinical Decision Support (CDS)
- Legislative Backdrop – 21st Century Cures Act
- FDA Proposed CDS Guidance
- Additional Digital Health Guidance Documents Update
- What's Next ?

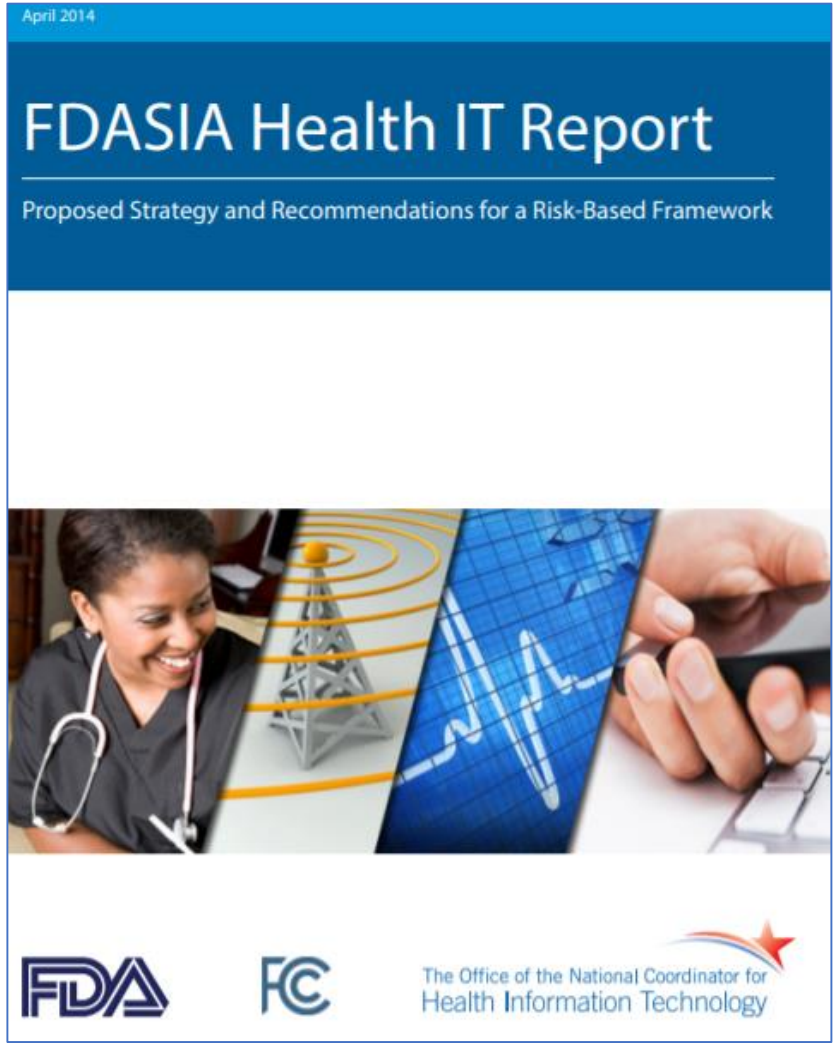
CDS – The Basics

- Software that accesses data (e.g., clinical guidelines, EHRs) and provides clinicians, staff, or patients with intelligently filtered information to enhance health and health care

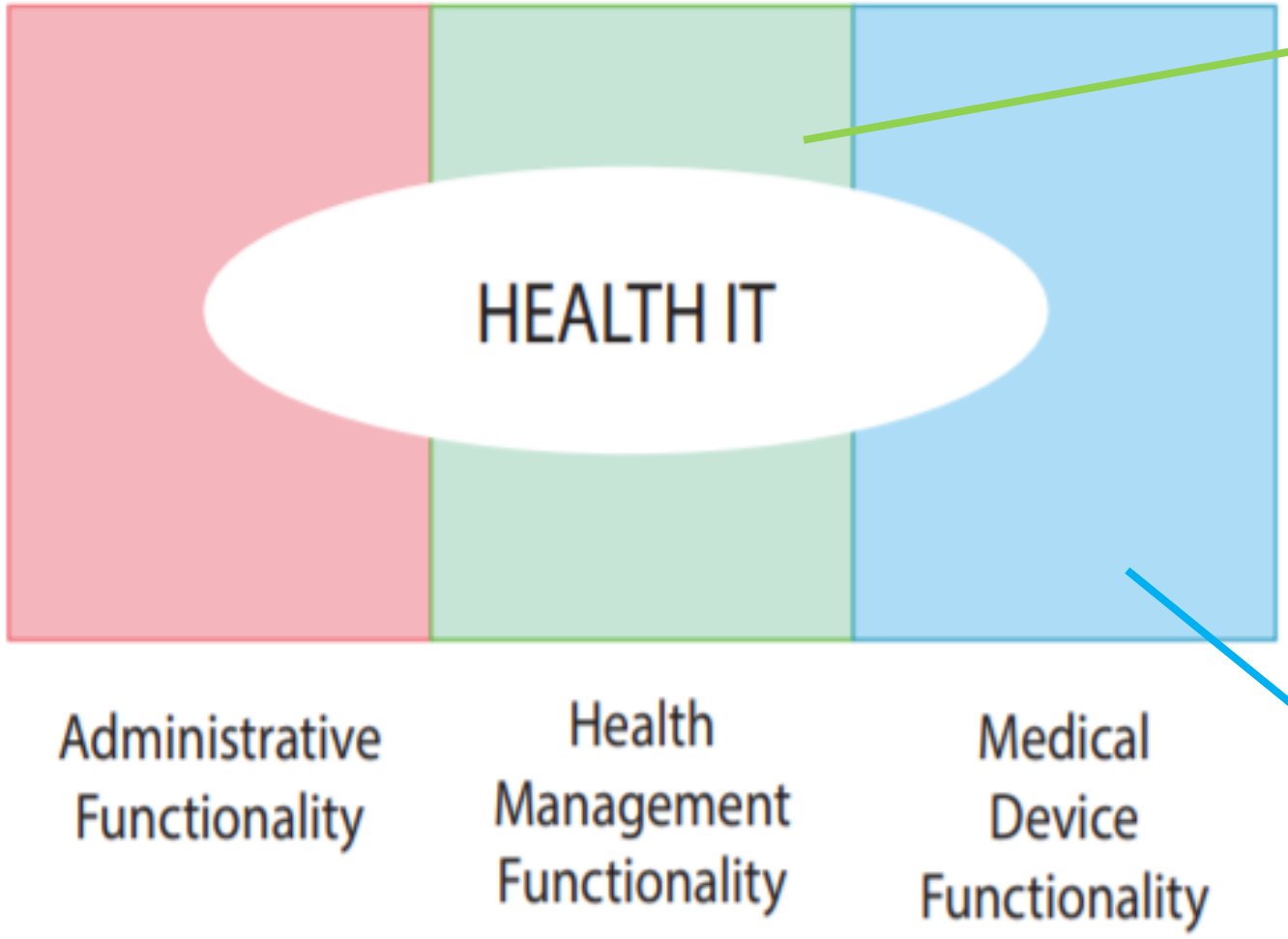


Legislative Backdrop

- FDASIA required FDA, in consultation with ONC and FCC, to develop regulatory framework for health IT
- 2014 Health IT Report
  - Hardware, software designed to support use by healthcare entities or patients for electronic creation/access/exchange of healthcare information
  - EHRs, claims processing, wireless medical devices, telehealth
  - Mobile apps



Legislative Backdrop – FDASIA



- Drug-drug interaction and drug-allergy contraindication alerts to avert adverse drug events;
- Most drug dosing calculations;
- Facilitation of access to treatment guidelines and other reference material that can provide information relevant to particular patients;
- Suggestions for possible diagnoses based on patient-specific information retrieved from a patient's EHR.

- Computer aided detection/diagnostic software;
- Remote display or notification of real-time alarms (physiological, technical, advisory) from bedside monitors;
- Radiation treatment planning;
- Robotic surgical planning and control;
- Electrocardiography analytical software.

Legislative Backdrop – 21st Century Cures Act

- Exempts certain software functions from the definition of “device” in the FDCA
  - Software for administrative support
  - Wellness apps and similar software
  - EHR software, to the extent not intended to analyze patient data or images
  - MDDS (medical device data system)

Legislative Backdrop – 21st Century Cures Act

- Exempts limited CDS from the definition of "device" in the FDCA

"(E) unless the function is intended to acquire, process, or analyze a medical image or a signal from an in vitro diagnostic device or a pattern or signal from a signal acquisition system, for the purpose of–

(i) displaying, analyzing, or printing medical information about a patient or other medical information (such as peer-reviewed clinical studies and clinical practice guidelines);

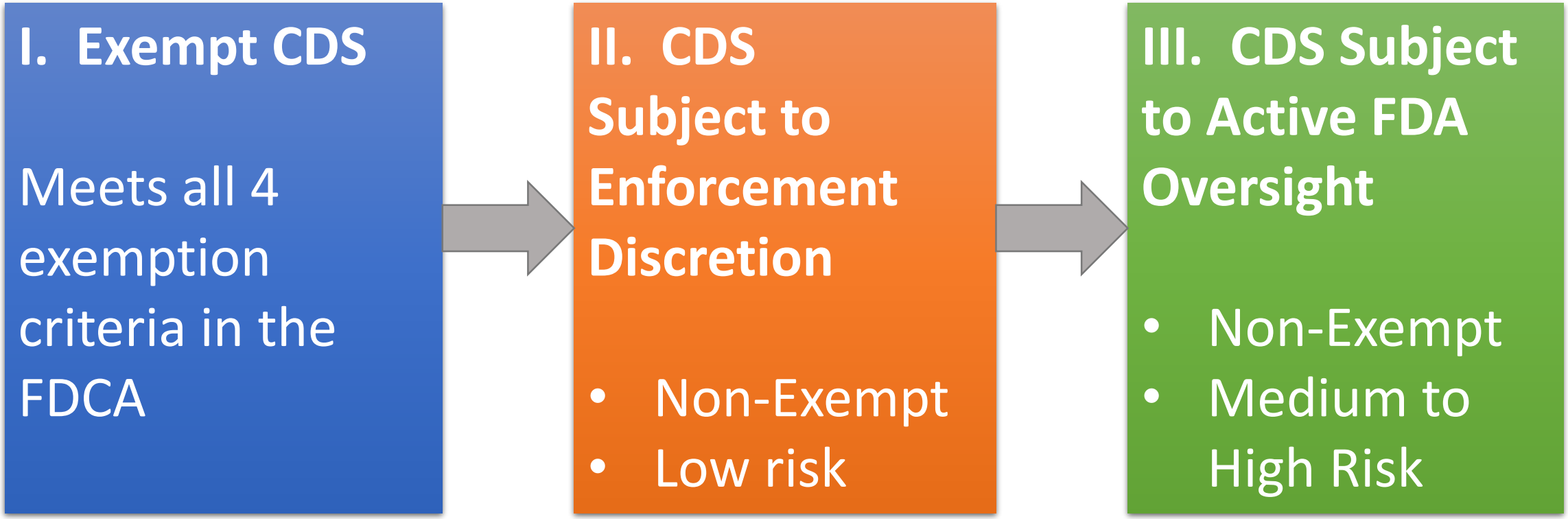
(ii) supporting or providing recommendations to a health care professional about prevention, diagnosis, or treatment of a disease or condition; and

(iii) 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."

-- 21st Century Cures Act, Sec. 3060(a)

FDA Draft Guidance – CDS categories

- FDA identifies categories of CDS software:



I. Exempt CDS – Criteria

- CDS is exempt from the definition of “device” if all 4 statutory criteria met:
  1. Not intended to acquire, process, or analyze signal from IVD or medical image
  2. Intended for the purpose of displaying, analyzing, or printing medical information
  3. Intended for the purpose of supporting or providing recommendations for HCP
  4. HCP can independently review the basis for the recommendation

Exempt CDS – Examples

- ✓ Software that compares patient signs, symptoms, or results with available practice guidelines (institutions-based or academic/clinical society-based) to recommend condition-specific diagnostic tests investigation, or therapy
- ✓ Software that provides HCPs with recommendations on the use of a IVD/medical device
- ✓ Software that suggests diagnostic test, based on clinical guidelines and patient's EHR. For example, software suggesting deficiency test before starting on an Rx drug
- ✓ Software that identifies drug-drug interactions – i.e., if patient presents symptoms and is already taking a drug
- ✓ Software that makes chemotherapeutic suggestions to an HCP based on patient history, test results, and patient characteristics, such as suggesting an FDA-approved chemotherapy for BRCA-positive individuals

Non-Exempt CDS – IMDRF Framework

- If not all criteria met, IMDRF risk-based approach applied
  - Seriousness of condition + significance of CDS output

Table 2. SaMD Categories established in IMDRF Framework

State of health care situation or condition	Significance of information provided by SaMD to health care decision		
	Treat or diagnose	Drive clinical management	Inform clinical management
Critical	IV	III	II
Serious	III	II	I
Non-serious	II	I	I

II. CDS Subject to Enforcement Discretion

- "Informs" + "non-serious" condition

Table 3. Summary of Regulatory Policy for CDS Software Functions

		Intended User is HCP		Intended User is Patient or Caregiver
IMDRF Risk Categorization	**Can the User Independently Review the Basis?***	**FDA Regulation**		**FDA Regulation**
Inform x Critical	Yes	Not a Device		Oversight Focus
	No	Oversight Focus		Oversight Focus
Inform x Serious	Yes	Not a Device		Oversight Focus
	No	Oversight Focus		Oversight Focus
Inform x Non-Serious	Yes	Not a Device		Enforcement Discretion**
	No	Enforcement Discretion**		Oversight Focus

CDS Subject to Enforcement Discretion – Examples

- ✓ Software intended for consumers that provides recommendations of potential allergens and common cold symptoms based on location-specific electronic health records, environmental conditions, and patient-reported outcomes
- ✓ Software intended for HCPs, where the basis for the recommendation is not disclosed, that analyzes patient information to determine which OTC allergy drug class is likely to be effective in alleviating the patient's seasonal allergies
- ✓ Machine-learning algorithm, for which the logic and inputs are not explained, that trends and classifies patient-specific data (*e.g.*, blood test results, weight) to alert HCPs to potential triggers for cholesterol management issues

III. CDS Subject to Active Regulation

- "Informs" + "non-serious" condition

Table 3. Summary of Regulatory Policy for CDS Software Functions

		Intended User is HCP		Intended User is Patient or Caregiver
IMDRF Risk Categorization	**Can the User Independently Review the Basis?***	**FDA Regulation**		**FDA Regulation**
Inform x Critical	Yes	Not a Device		Oversight Focus
	No	Oversight Focus		Oversight Focus
Inform x Serious	Yes	Not a Device		Oversight Focus
	No	Oversight Focus		Oversight Focus
Inform x Non-Serious	Yes	Not a Device		Enforcement Discretion**
	No	Enforcement Discretion**		Oversight Focus

CDS Subject to Active Regulation – Examples

- Software that analyzes patient medical images. E.g.:
  - Uses patient images (CT, MR) to create individual treatment plan for review by HCP
  - Software that analyzes images of digital slides (digital pathology) to perform cell counts and morphology reviews
  - Analyzes dimensions of skin lesion to provide suggestion of whether lesion is benign/ malignant
- Software that queries multiple genetic variants against reference databases to make patient-specific recommendations about the significance of a patient's variants

Additional Guidance Documents Updated

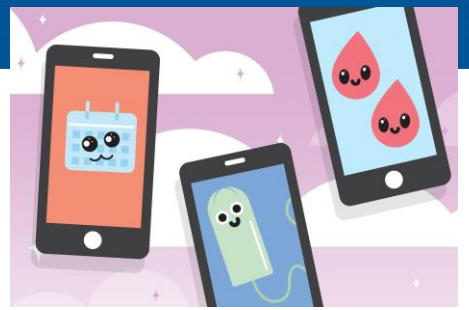
- FDA also updated guidance documents in light of the 21st Century Cures Act:
  - *Off-the-Shelf Software Use in Medical Devices*
  - *General Wellness: Policy for Low Risk Devices*
  - *Mobile Medical Applications*
  - *Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices*
- When is medical device software not a "device" requiring FDA clearance or approval?

Off-the-Shelf Software in Medical Devices

- Laboratory Information Systems (LIS) and Laboratory Information Management Systems (LIMS) functions intended for administrative support of laboratories and/or for transferring, storing, converting formats, or displaying clinical laboratory test data and results are not within the definition of “device”

  - However, some LIS and LIMS include software functions remain device functions, including software functions that analyze medical device data in order to provide a notification or flag (*e.g.*, that a parameter is out of range) and such functions will continue to be regulated as devices

General Wellness: Policy for Low Risk Devices

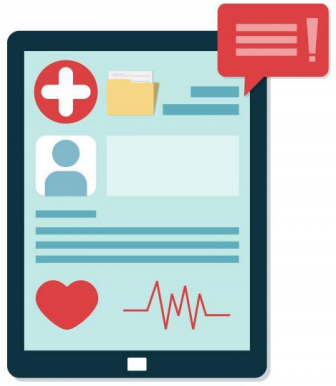


- Intended use for maintaining or encouraging a “healthy lifestyle”
  1. Are intended for only general wellness use
     - software with healthy lifestyle claims, such as weight management, physical fitness, relaxation or stress management, mental acuity, self-esteem, sleep management, or sexual function, are not devices when **not** related to the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition
       - If related to diagnosis, cure, mitigation, prevention, or treatment of a disease or condition → device.
  2. Present a low risk to the safety of users

- Examples:
  - App that plays music to “soothe and relax” an individual and to “manage stress”
  - App that solely monitors and records daily energy expenditure and cardiovascular workout activities to “allow awareness of one’s exercise activities to improve or maintain good cardiovascular health”
  - App that monitors and records food consumption to “manage dietary activity for weight management and alert the user, health care provider, or family activity for weight management and alert the user, health care provider, or family member of unhealthy dietary activity”

Mobile Medical Applications

- Software functions that are intended to transfer, store, convert formats, or display electronic patient records that are the equivalent of a paper medical chart are not devices, if three criteria are met:
  1. Such records were created, stored, transferred, or reviewed by health care professionals (HCPs), or by individuals working under supervision of such professionals, and
  2. Such records are part of information technology certified under a program of voluntary certification kept or recognized by the Office of the National Coordinator for Health Information Technology (ONC) under section 3001(c)(5) of the Public Health Service Act ("ONC Health IT Certification Program"), and
  3. Software functions are not intended for interpretation or analysis of patient records, including medical image data, for the purpose of the diagnosis, cure, mitigation, prevention, or treatment of a disease or condition.



Examples:

- Apps that provide patients with simple tools to organize and track their health information
- Apps that are specifically marketed to help patients document, show, or communicate to providers potential medical conditions
- Apps that enable, during an encounter, a health care provider to access a patient's personal health record that is hosted on a web-based or other platform

Medical Device Data Systems, Medical Image Storage Devices, and Medical Image Communications Devices

- Software functions that are solely intended to transfer, store, convert formats, and display medical device data and results, including medical images, waveforms, signals, or other clinical information are not devices and thus are not subject to FDA regulatory requirements
- ***However***, software functions that analyze or interpret medical device data in addition to transferring, storing, converting formats, or displaying clinical laboratory test or other device data and results remain subject to FDA's regulatory oversight
  - For example, software functions intended to generate alarms or alerts or prioritize patient-related information on multi-patient displays involve analysis or interpretation of laboratory test or other device data and results are not excluded from the definition of "device" under section 520(o)(1)(D) of the FDCA

What's Next … AI in Digital Health

- Continued market adoption of digital health in healthcare

Streamline HC institution workflow

Mobile apps in clinical trials

Monitor patients in real time

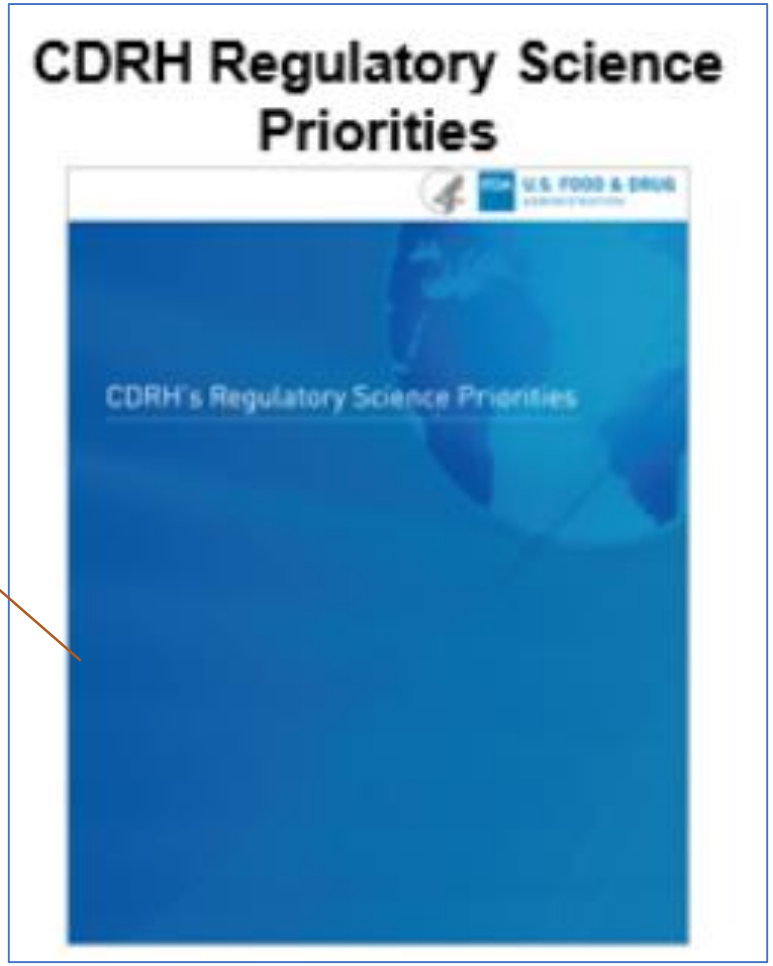
Diagnose patient from clinical images

- FDA adopting policies for novel technology, such as artificial intelligence (AI)/machine learning (ML)
  - FDA proposed white paper for AI/ML software that adds premarket submission mechanism to accommodate software that evolves as it learns
  - Focused review of changes (as opposed to a new 510(k) submission)
- Companies currently submitting CDS/AI software as *de novo* requests:
  - CDS uses AI algorithm to scan CT images for indicators associated with stroke, and sends a text notification to a neurovascular specialist if it identifies a potential large vessel blockage
  - CDS uses AI algorithm to scan X-ray images for a common type of wrist bone fracture. Software can be fed images of adult wrists and highlight regions with potential fracture

What's Next … Cybersecurity as a Threat

"Innovative methods and technologies will need to be developed to protect the integrity of medical device performance and enhance security as devices become more interconnected and autonomous which makes them increasingly vulnerable to cyberattacks and unobserved malfunction.

Medical device stakeholders need a firm understanding of cybersecurity considerations, risks, and mitigation options at the device and systems levels."



Questions?

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