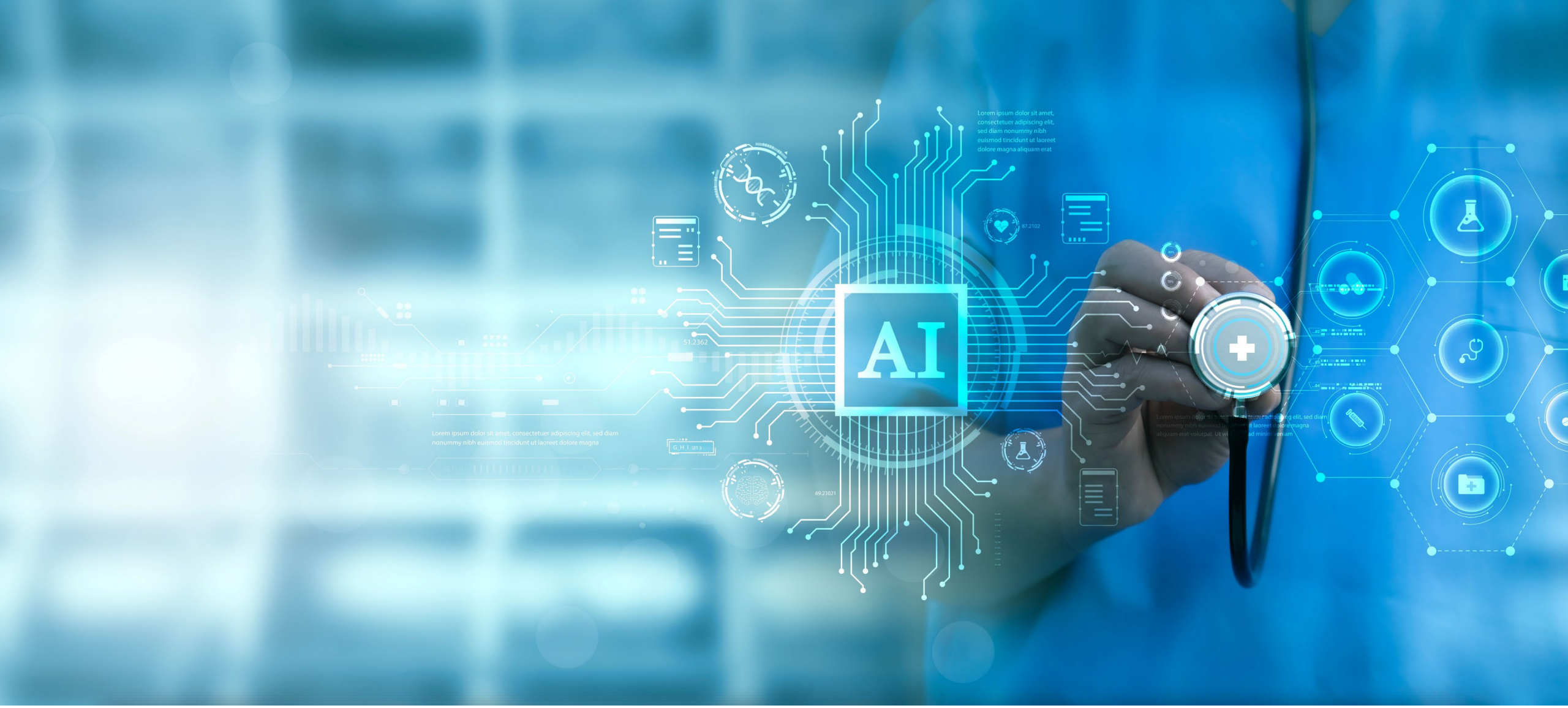
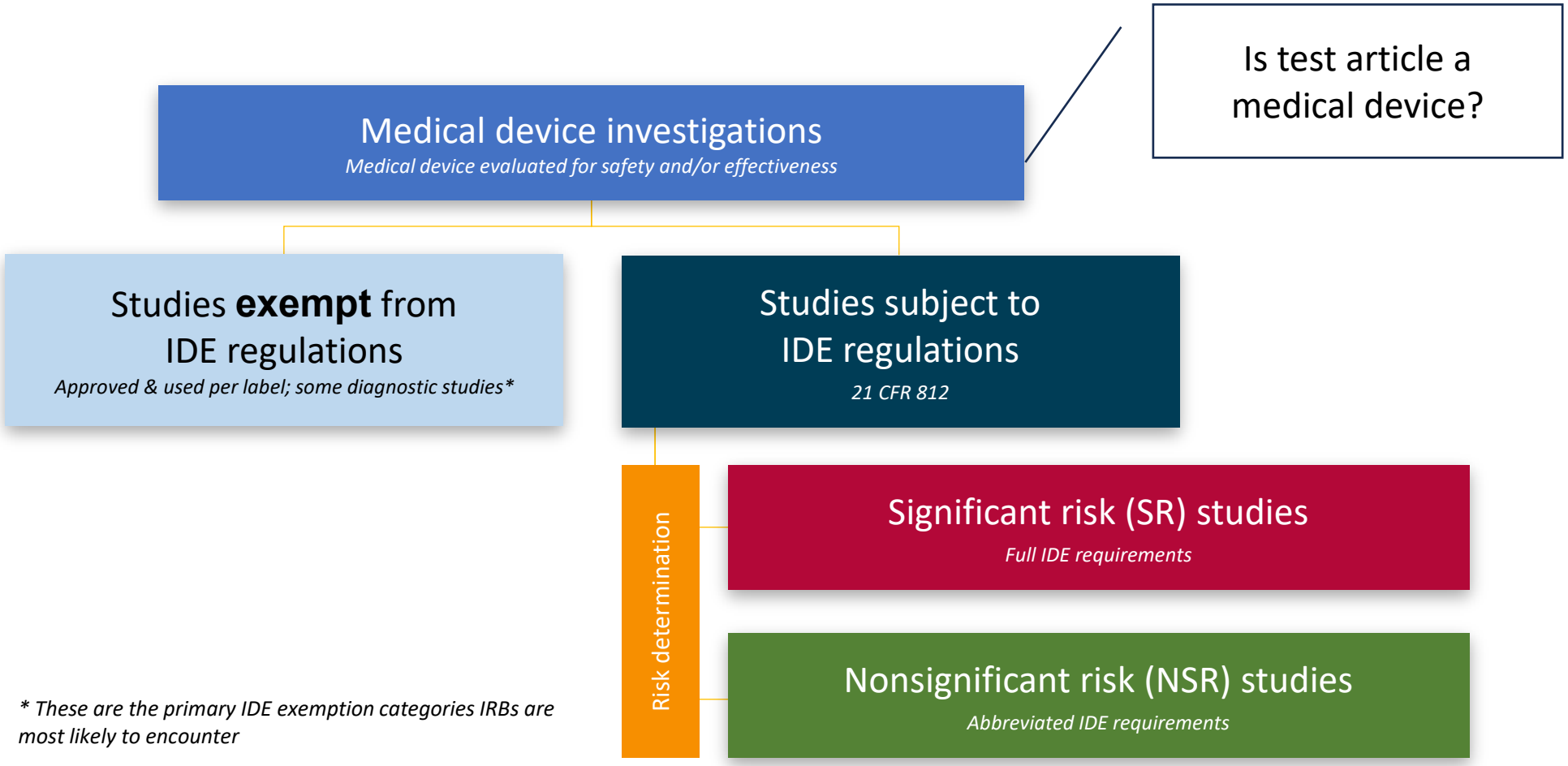


FDA AI/ML Enabled Software as a Medical Device (SaMD)

Belinda Smith, MS, RD, CCRC

2024

Framework



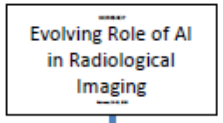
** These are the primary IDE exemption categories IRBs are most likely to encounter*

FDA's Collaborative Patient-Centered Approach to AI/ML-Enabled Devices

Published AI/ML-SaMD Discussion Paper

2019

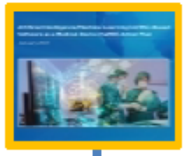
First joined Collaborative Community related to AI/ML



Public Workshop on AI/ML in Radiological Imaging

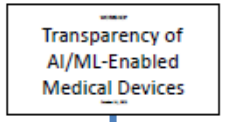
2020

PEAC Mtg on Patient Trust in AI/ML Devices



Published AI/ML Medical Device Software Action Plan

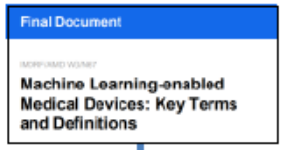
2021



Public Workshop on Transparency of AI/ML Devices

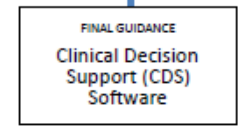
Posted List of Currently Marketed AI/ML Devices

Published GMLP Guiding Principles



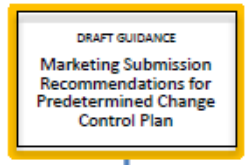
2022

Contributed to IMDRF's Key Terms and Definitions



Published Final Guidance: Clinical Decision Support

AI/ML PCCP Guidance



2023

We're working collaboratively with stakeholders to build a proactive, patient-centered approach to AI/ML-enabled devices that promotes health equity.

www.fda.gov/digitalhealth

Matthew Diamond, MD, PhD, Digital Health Center of Excellence, FDA

FDA AI/ML Action Plan

FDA determined "AI/ML-based software, when intended to treat, diagnose, cure, mitigate, or prevent disease or other conditions, are medical devices under the FD&C Act" and classified as *"Software as a Medical Device" (SaMD)*. Therefore, the research is FDA-regulated.

SaMD may use AI or ML

- A SaMD can best be described as software that utilizes an algorithm (logic, set of rules, or model) that operates on data input (digitized content) to produce an output that is intended for medical purposes as defined by the SaMD manufacturer.*
- Machine Learning (ML) may be used to design and train software algorithms to learn patterns from data, including classification, inference, matching previous patterns, predicting future outputs, etc., without being explicitly programmed to reach a particular answer or conclusion.
- This results in an ML model which may be applied clinically.

*2017 FDA SaMD Clinical Evaluation Guidance

Use of Artificial Intelligence/Machine Learning

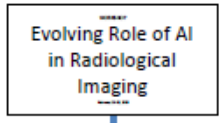
- COViage, a software prediction system, assesses whether hospitalized COVID-19 patients are at high risk of needing intubation.

- However, AI-enabled products have sometimes resulted in inaccurate, even potentially harmful, recommendations for treatment due to bias in the information used to build or train the model.

- Algorithms developed without considering geographic diversity, variables such as disease prevalence and socioeconomic differences, may not perform as well as they should (e.g., an algorithm developed to help detect melanoma is trained heavily on images of patients with lighter skin tones may fail analyze lesions in people of color).

FDA's Collaborative Patient-Centered Approach to AI/ML-Enabled Devices

Published AI/ML-SaMD Discussion Paper



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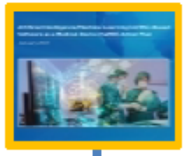
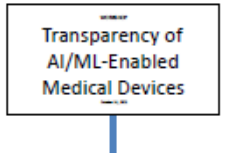
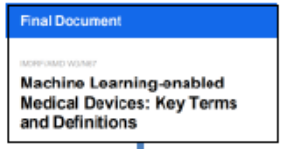


Published AI/ML Medical Device Software Action Plan



Public Workshop on Transparency of AI/ML Devices



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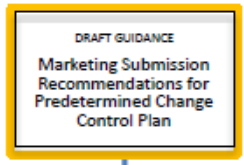

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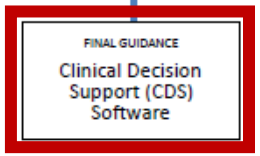

2023

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www.fda.gov/digitalhealth

Matthew Diamond, MD, PhD, Digital Health Center of Excellence, FDA

Your Clinical Decision Support Software: Is It a Device?

The FDA issued a guidance, Clinical Decision Support Software, to describe the FDA's regulatory approach to Clinical Decision Support (CDS) software functions. This graphic gives a general and summary overview of the guidance and is for illustrative purposes only. Consult the guidance for the complete discussion and examples. Other software functions that are not listed may also be device software functions. *

Your software function must meet all four criteria to be Non-Device CDS.

Summary interpretation of CDS criteria

1. Your software function does **NOT** acquire, process, or analyze medical images, signals, or patterns.
2. Your software function displays, analyzes, or prints medical information normally communicated between health care professionals (HCPs).
3. Your software function provides recommendations (information/options) to a HCP rather than provide a specific output or directive.
4. Your software function provides the basis of the recommendations so that the HCP does not rely primarily on any recommendations to make a decision.

Your software function may be non-device CDS.

Non-Device Examples

Non-Device examples display, analyze, or print the following examples of medical information, which must also not be images, signals, or patterns:

- Information whose relevance to a clinical decision is well understood
- A single discrete test result that is clinically meaningful
- Report from imaging study

AND

Non-Device examples provide:

- Lists of preventive, diagnostic, or treatment options
- Clinical guidelines matched to patient-specific medical info
- Relevant reference information about a disease or condition

AND

Non-Device examples provide:

- Plain language descriptions of the software purpose, medical input, underlying algorithm
- Relevant patient-specific information and other knowns/unknowns for consideration

Device Examples

Device examples acquire, process, or analyze:

- Signal acquisition systems
- In vitro diagnostics
- Magnetic resonance imaging (MRI)
- Next Generation Sequencing (NGS)
- Continuous Glucose Monitoring (CGM)
- Computer aided detection/diagnosis (CADe/CADx)

OR

Device examples display, analyze or print:

- Continuous signals/patterns
- Medical images
- Waveforms (ECG)
- More continuous sampling (aka – a signal or pattern)

OR

Device examples provide:

- Risk scores for disease or condition
- Probability of disease or condition
- Time-critical outputs

OR

Device examples:

- Basis of recommendations is not provided

Your software function is a device.

***Disclaimer:** This graphic gives a general overview of Section IV of the guidance ("Interpretation of Criteria in Section 520(o)(1)(E) of the FD&C Act"). Consult the guidance for the complete discussion. The device examples identified in this graphic are illustrative only and are not an exhaustive list. Other software functions that are not listed may also be device software functions.

Clinical Decision Support Software (CDSS)

9/2022 CDSS Guidance outlines FDA's approach

The determination focuses on whether the software will provide options or make directive determinations and the basis of recommendations is transparent, so the health care provider can independently review and DOES NOT RELY primarily on software to make clinical care decisions.

Some AI programs, are referred to as "black-box" models because the algorithms are derived from large datasets using complex techniques and reflect underlying patterns that may be too convoluted for a person, including the initial programmer, to understand.

AI/ML Algorithms Example from 2022 Guidance

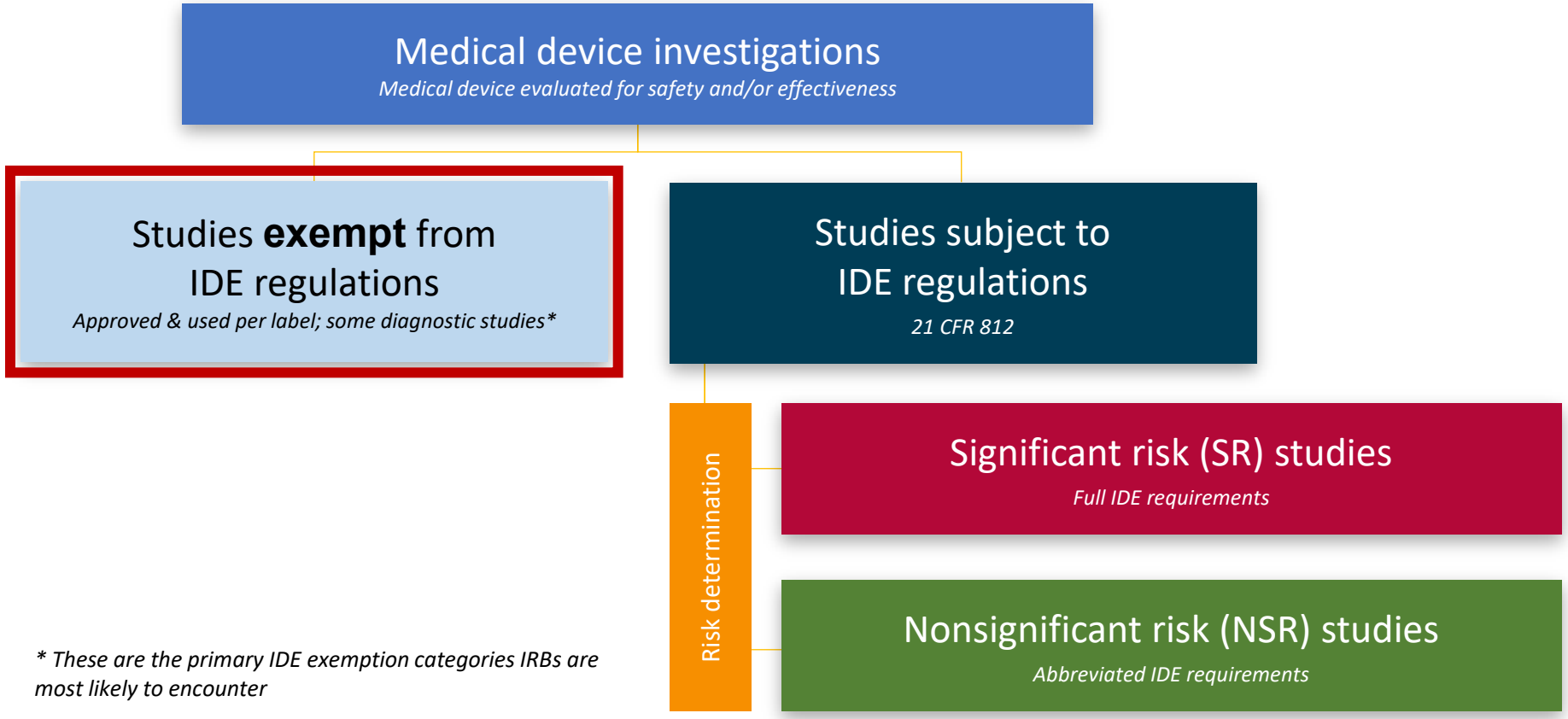
- Software function that analyzes patient-specific medical information found in the medical record, including the most recent mammography report findings, in order to provide a list of follow-up options for the Health Care Provider (HCP) to consider following a patient's annual mammogram.
- The software algorithm is trained on a large dataset of 100,000 cases from 10 clinical sites, with summary performance based on subsequent cancer detection rates with supplemental imaging and biopsy. The product labeling provides information on the purpose of the software, the intended user and patient population, and a description of the software outputs.

AI/ML Algorithms Example from 2022 Guidance

- While the HCP is informed that an algorithm was trained on a large dataset with supplemental imaging and biopsy, specific details on the independence of the development and validation datasets, such as the distribution of cases from different sites, breast density, ethnicity, or other important factors, are not available to the HCP. Without this information, the HCP will not be able to assess if the results are generalizable…
- an HCP is not able to independently review the basis for the recommendations that the software function provides. As a result, the software function is a device.

Does not meet Criteria 4 – IS A MEDICAL DEVICE

Framework



** These are the primary IDE exemption categories IRBs are most likely to encounter*

IDE Exempt Studies

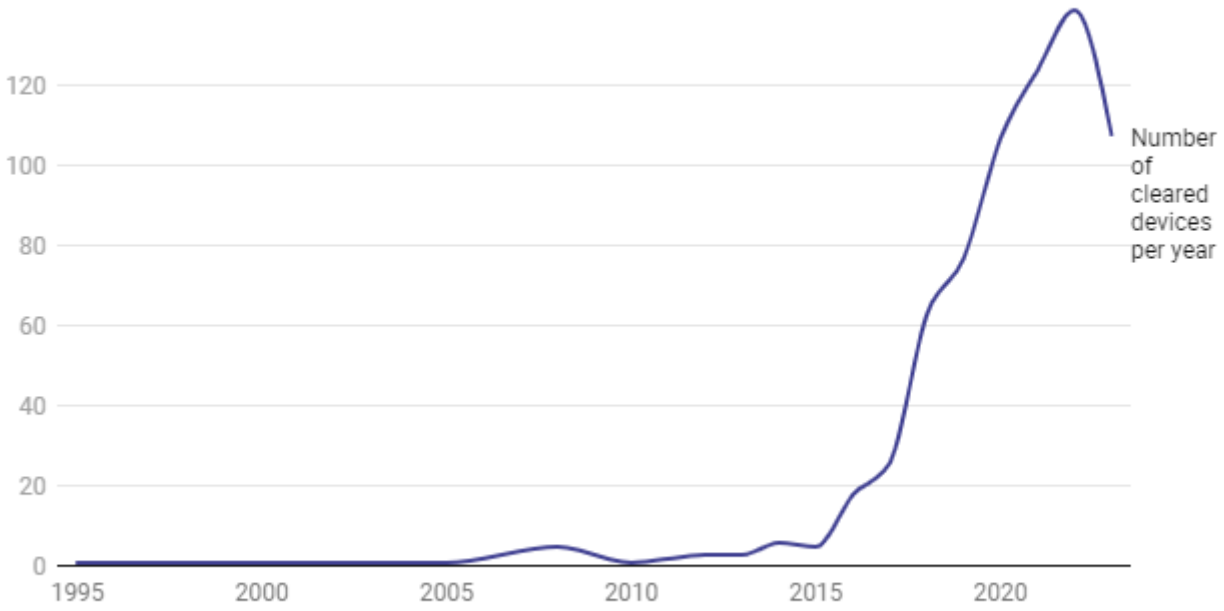
- Do not require submission of an IDE application to FDA
- Typically qualify for Expedited Review
- Still subject to FDA Parts 50 (Informed Consent) and 56 (IRB Review) Regulations
- Types of exempted studies given in 21 CFR 812.2(c)

- ~700 List of FDA Cleared or Approved AI/ML Devices

ML models have ranged in complexity from shallow (less than 2 hidden layers) models to more complex Deep Learning Models (DLM).

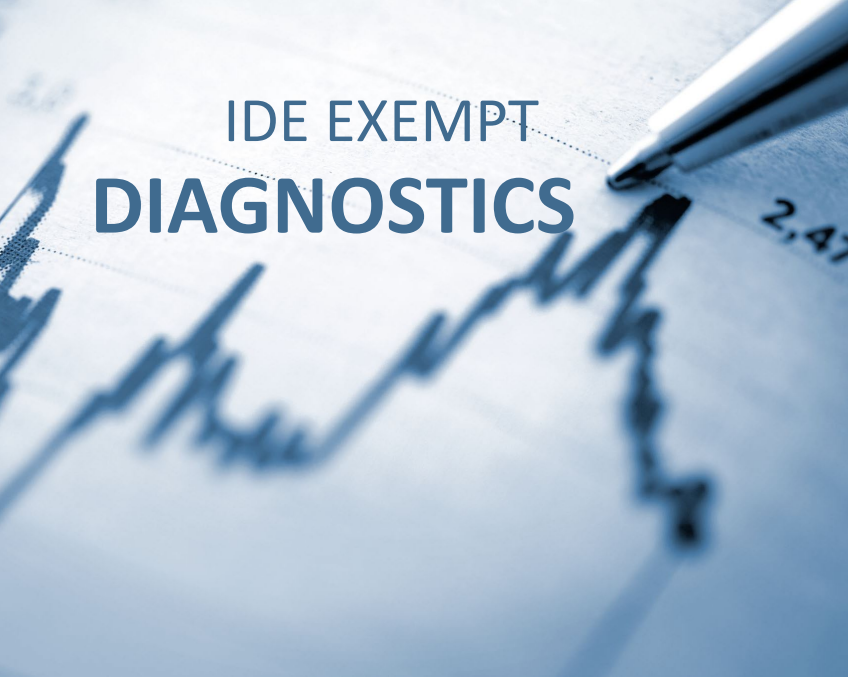
Criteria for IDE exemption under 21 CFR 812.2(c)(2): Commercial device used in accordance with its labeling

The number of FDA-authorized AI/ML devices by year, based on the decision date, through July 30, 2023.



Note: 2023 data is only through July 30.

Chart: Elise Reuter • Source: FDA, AI/ML-Enabled Medical Devices • Get the data • Created with Datawrapper



Criteria for IDE exemption as a Diagnostic 21 CFR 812.2(c)(3):

If this SaMD is being created with existing images or leftover tissues and results will not be returned to subjects or their clinicians, can the IRB use the "IDE Exemption as an in-vitro diagnostic" to determine study exempt from IDE requirements?

ORI SUGGESTED LIMITATIONS

a. Secondary Use - using existing data, images, etc.
b. No interaction or intervention with human subjects
c. Not providing images, data to a software developing company

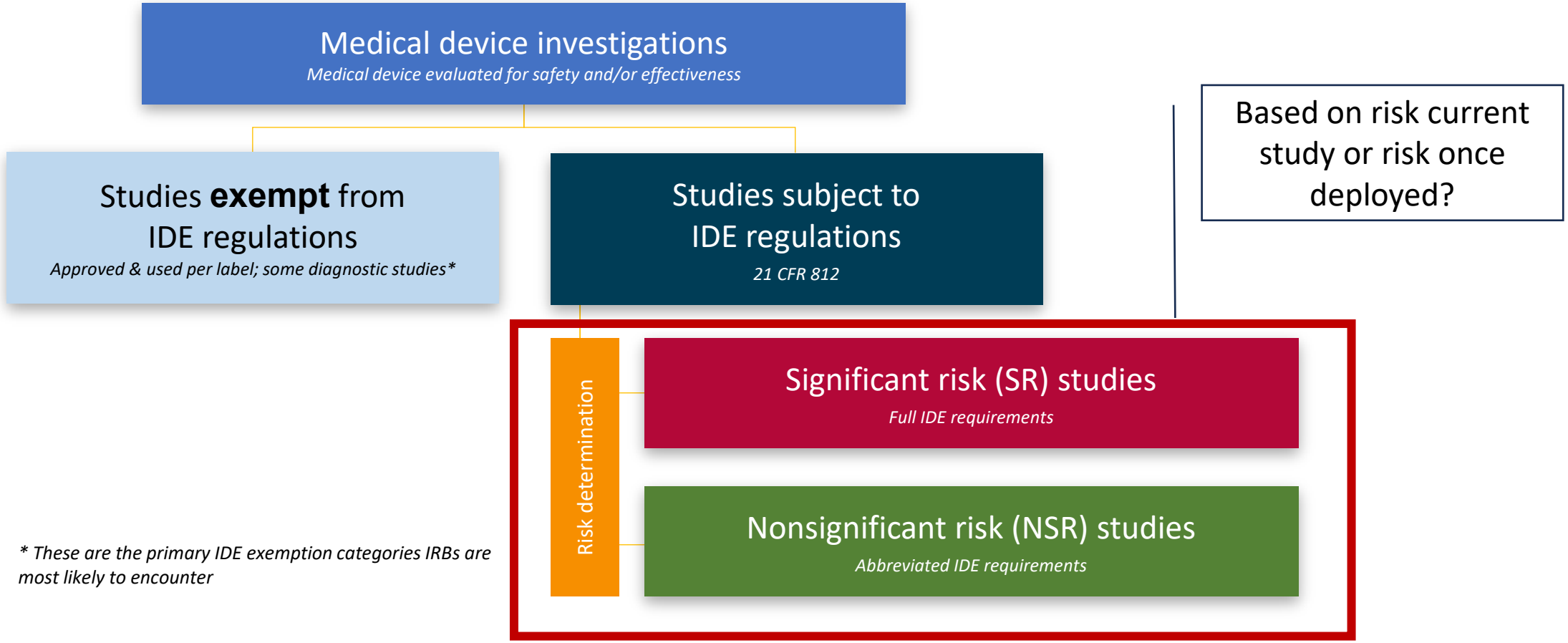
Who is considered a software developer depends on where output will be deployed?

Policy for Device Software Functions and Mobile Medical Apps

Licensed practitioners are, under certain circumstances, not within the definition of a device manufacturer if developing software solely for their individual or own group practice only.

If there is an intent to make a product generally available or for a product to be generally used by other physicians, a developer who is a licensed practitioner would be considered a manufacturer.
In this case, best practice may be to obtain SR/NSR.

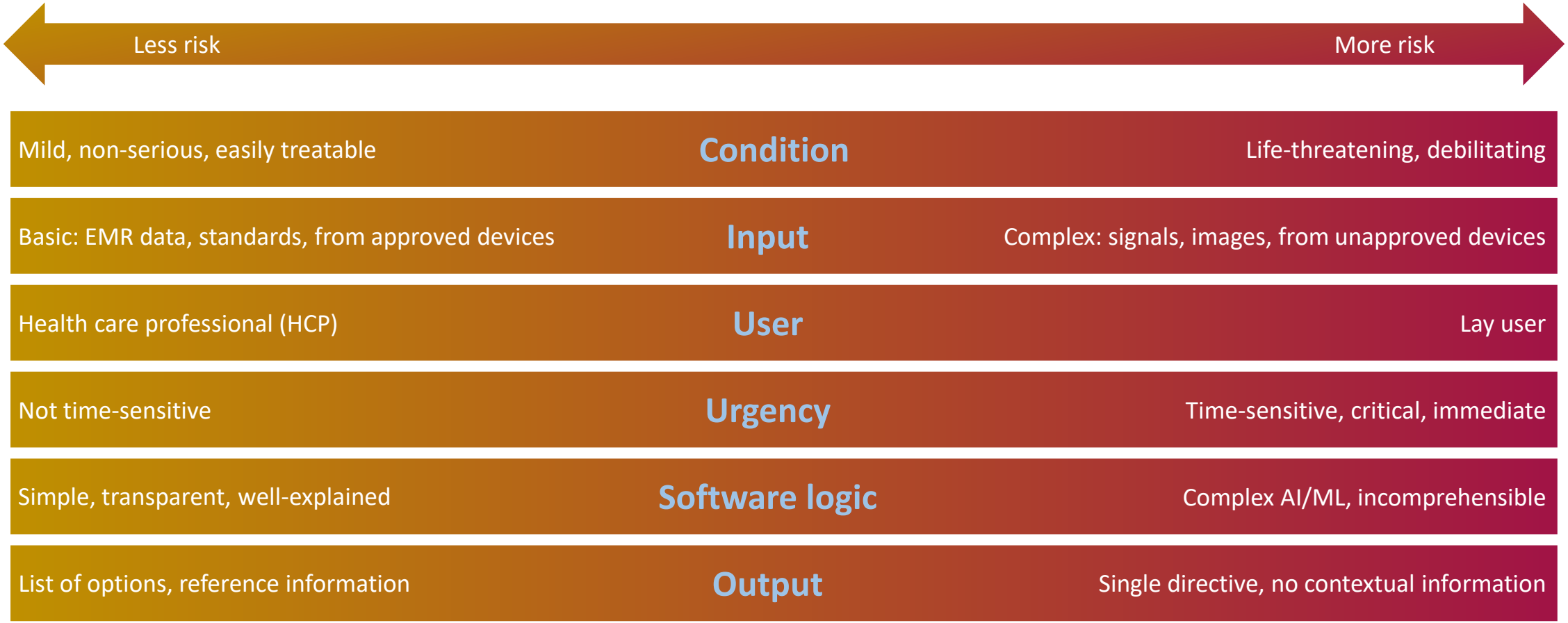
Framework



** These are the primary IDE exemption categories IRBs are most likely to encounter*

SaMD: NSR or SR?

What is the nature of harm that may result from use of the device or failure of the device?



Resources for Digital Health

- FDA Digital Health Policy Navigator*
- Contact: Digital Health Center of Excellence, FDA
- Webpage: AI/ML-enabled medical devices
- FDA guidance: Clinical Decision Support Software (2022)*
- FDA guidance: General Wellness – Policy for low-risk devices (2019)*

**Not written for IRBs or clinical trials. We must extrapolate basic principles in order to apply them to IDE exempt determinations.*

ADVANCE

Faculty Guidelines Research Recommendations

Research Recommendations

Generative AI tools have the potential of advancing and enhancing research and scholarly endeavors when used responsibly. These recommendations are for all faculty, staff and trainees who engage in this work.

What privacy concerns arise in using generative AI in research?

Inputting any research data into a generative AI tool renders that data available in the AI tool and its use. Accordingly, data privacy review is needed before any Protected Data (AR 10.7) is entered into a generative AI tool (whether the tool is publicly available or not) to ensure that the tool's data privacy and security program complies with all applicable laws and university guidelines. This process can be initiated by contacting the UK Information Technology Services Governance, Risk and Compliance (GRC) team at GRC@uky.edu.

Generative AI tools that are public and available for use by anyone pose elevated risks to privacy when entering research data, in particular protected health information (PHI), personal identifying information or other personal information protected by law such as FERPA, and any proprietary information.

Unless the UKHC InfoSec Data Sharing Committee has confirmed the AI tool is HIPAA compliant and supports PHI input, do not put research data containing PHI into an open-source AI tool. Additionally, other non-public or proprietary research data should not be placed into an open- source AI tool without UK ITS GRC approval.