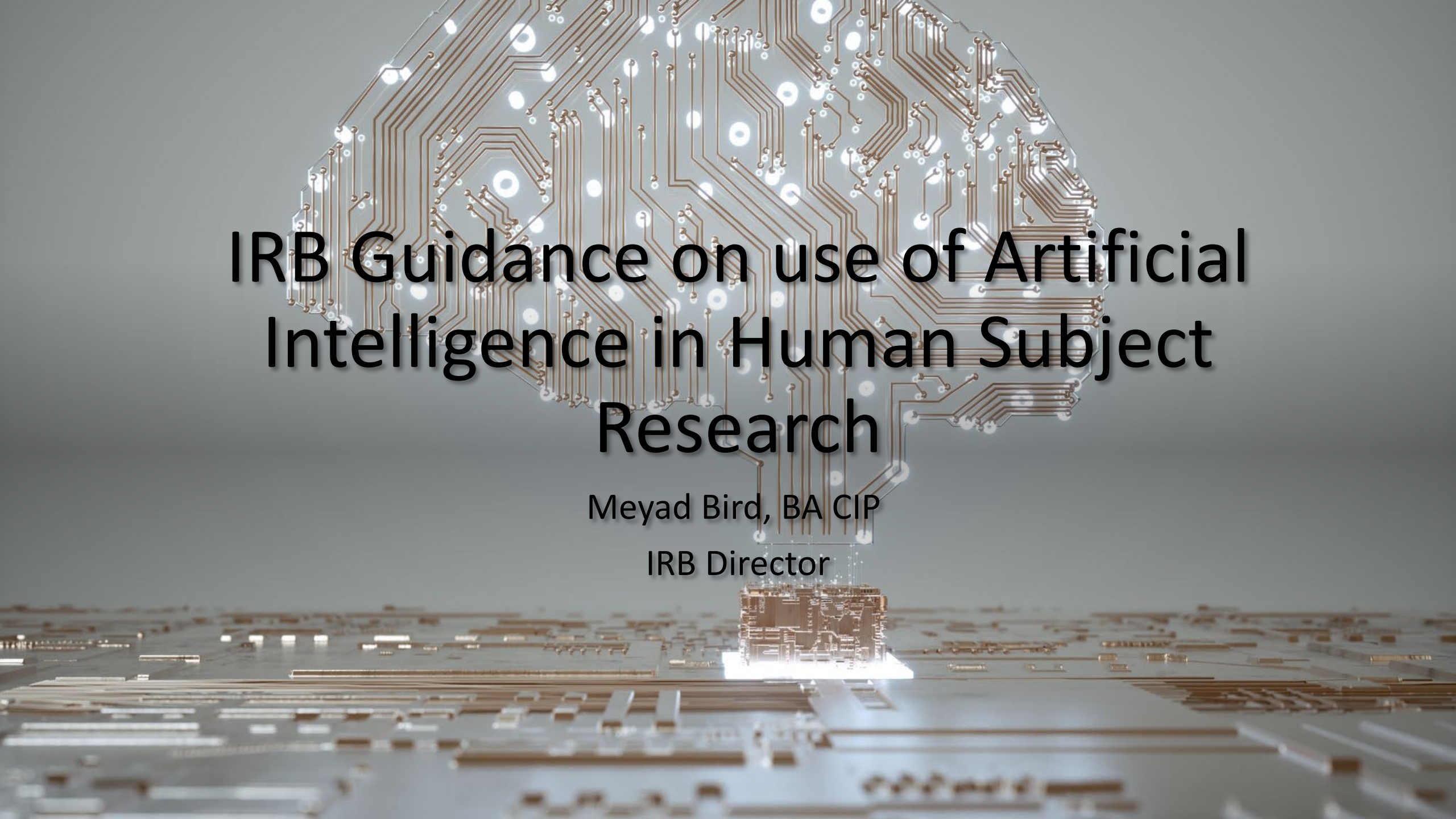


IRB Guidance on use of Artificial Intelligence in Human Subject Research

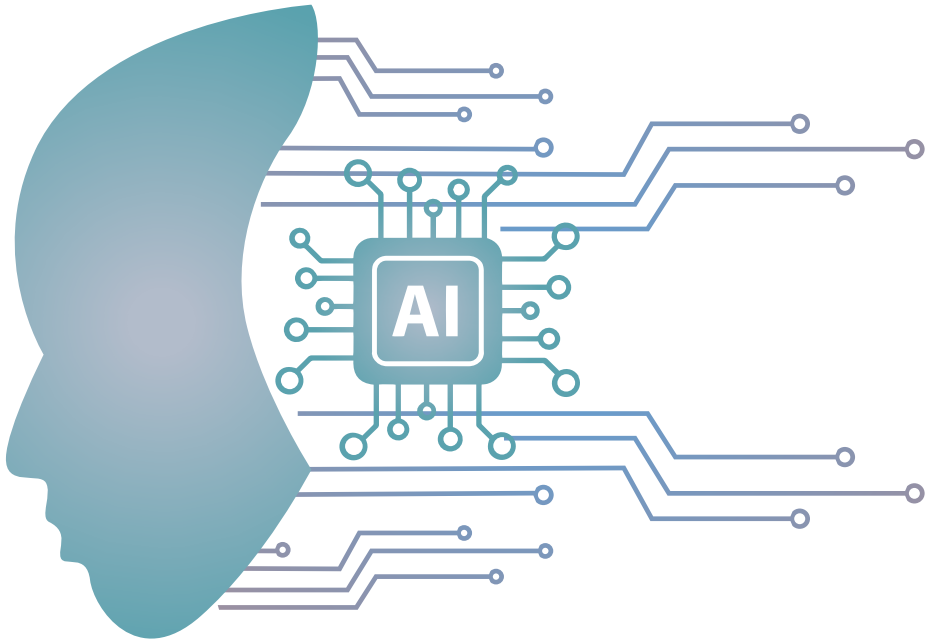
Meyad Bird, BA CIP

IRB Director

UT Southwestern Medical Center

Artificial Intelligence (AI)

- The science and engineering of making intelligent machines, especially intelligent computer programs
- Can use different techniques, including models based on statistical analysis of data, expert systems that primarily rely on if-then statements, and machine learning.



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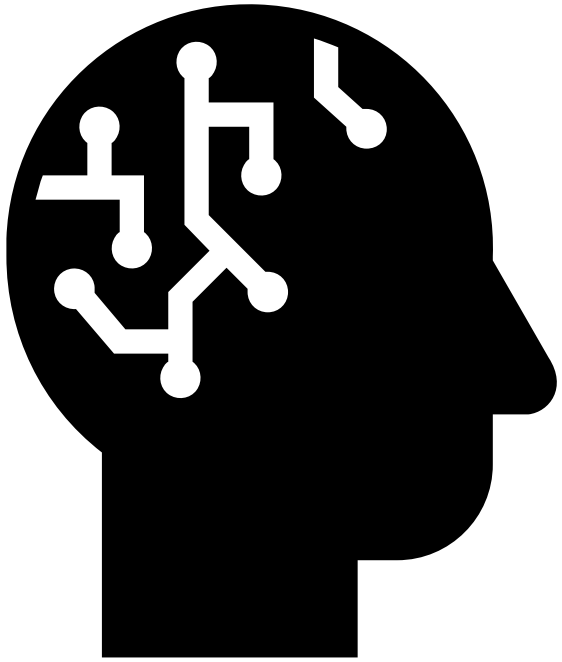
Machine Learning (ML)



- Is an artificial intelligence technique that can be used to design and train software algorithms to learn from and act on data.
- Software developers can use machine learning to create an algorithm that is ‘locked’ so that its function does not change, or ‘adaptive’ so its behavior can change over time based on new data.

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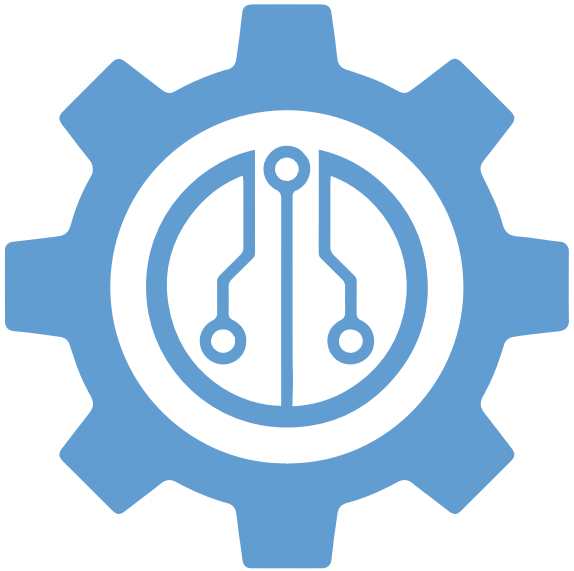
When is IRB Review required?

FDA – 21 CFR 56

Clinical Evaluations and Investigations of devices including early feasibility studies



OHRP – 45 CFR 46

Interaction/intervention or when using, analyzing, generating identifiable information

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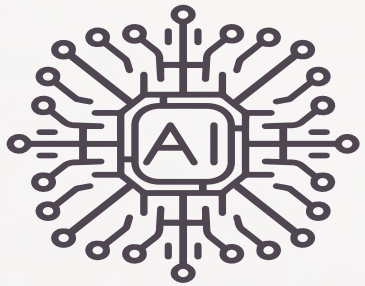
Criteria to consider



Is it a medical device (FDA)?

Is it research?

Does it involve human subjects?

Is it exempt?

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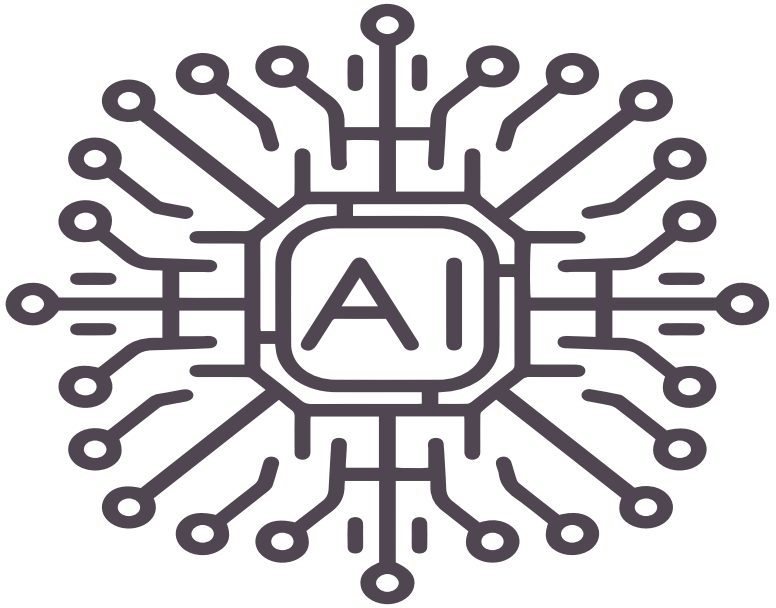
Is the software a Medical Device?



Is it a medical device (FDA)?

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Is the software a Medical Device?

- Software that is intended to be used for one or more medical purposes that perform these purposes without being part of a hardware medical device.
- IRB review is required

Is it a medical device (FDA)?

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Is the use of the software research?

Is it research?

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Is the use of the software research?

- Research – is a **systematic investigation** (including development, testing, and/or evaluation, designed to contribute to **generalizable knowledge**
  - Systematic Investigation – a careful or detailed inquiry or examination of information that involves a system, method, or plan.
  - Generalizable knowledge – widely applicable
    - Non-generalizable AI– intended use of the algorithm is limited to the application to the original data set
    - Generalizable AI – intended to be built as a tool to be applied to a broad population or not-yet collected data

Is it research?

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Does it involve human subjects

Does it involve human subjects?

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Does it involve human subjects

- Human subject is defined as:

- A **living individual** about whom an investigator (whether professional or student) is conducting research:
  - Obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or
  - Obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimen
    - To develop AI Tools

Does it involve human subjects?

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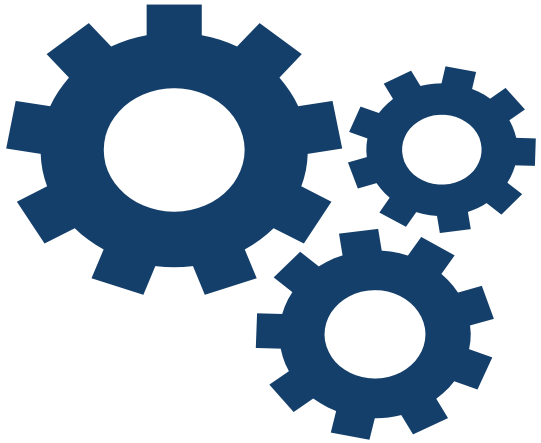
Is it exempt research?

- If software is a medical device, it cannot be exempt.



Is it exempt?

When IRB approval is **not** required

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EBP/Non-Investigational

Using evidence-based models that are SOC/non investigational

Quality Improvement

Limited to improving clinical workflows, health care delivery, and quality

Limited Use

Limited usefulness to own department/unit/clinic

Developed by practitioner

*Models developed by a practitioner is **for their use solely***

IRB Considerations/Protocol Details

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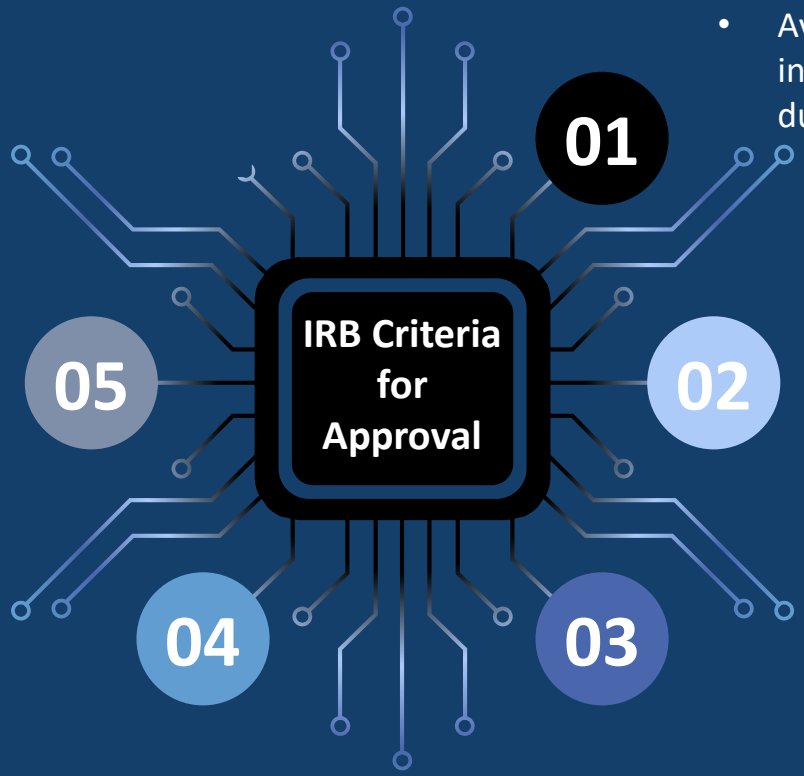

Equitable selection of subjects

- Include populations that are impacted by the findings
- The data set should be large and diverse for target population
- Avoid unnecessary inclusion/exclusion of certain groups due to inconvenience

Confidentiality

- How datasets will be maintained confidentially
- How re-identifiability is minimized
- How internal and external datasets that will be pooled are maintained confidentially
- Considerations are made for BAAs, DUAs, etc.

Informed Consent

- Was consent obtained for future use in this manner
- Are there state laws regarding use of data/images (e.g., Cause of Death/National Death Index, HIV, mental health, incriminating data, etc.)
- Is waiver of consent appropriate

Privacy

- Adhering to HIPAA requirements
- Identifying what PHI/PII will be used and by whom
- Additional protections for small populations
- Extra protections for sensitive data

Data Monitoring

- Model iterations, data shift, version changes,
- Post deployment monitoring to identify harms
- Process to mitigate biases
- Having a plan to monitor for anticipated problems and how they will be handled

Clinical Investigation vs Clinical Evaluation

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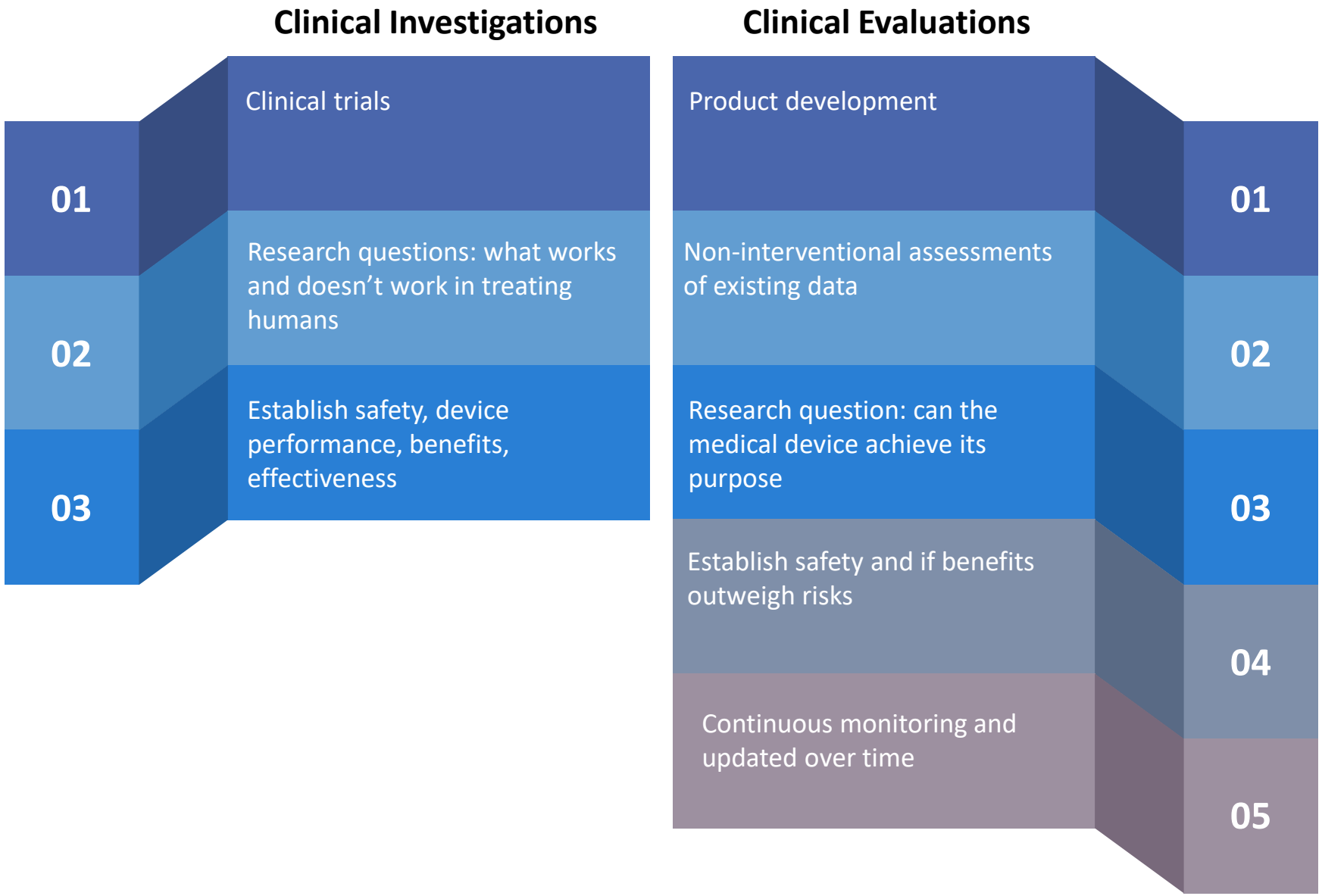

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Software as Medical Device Determinations (SaMD)

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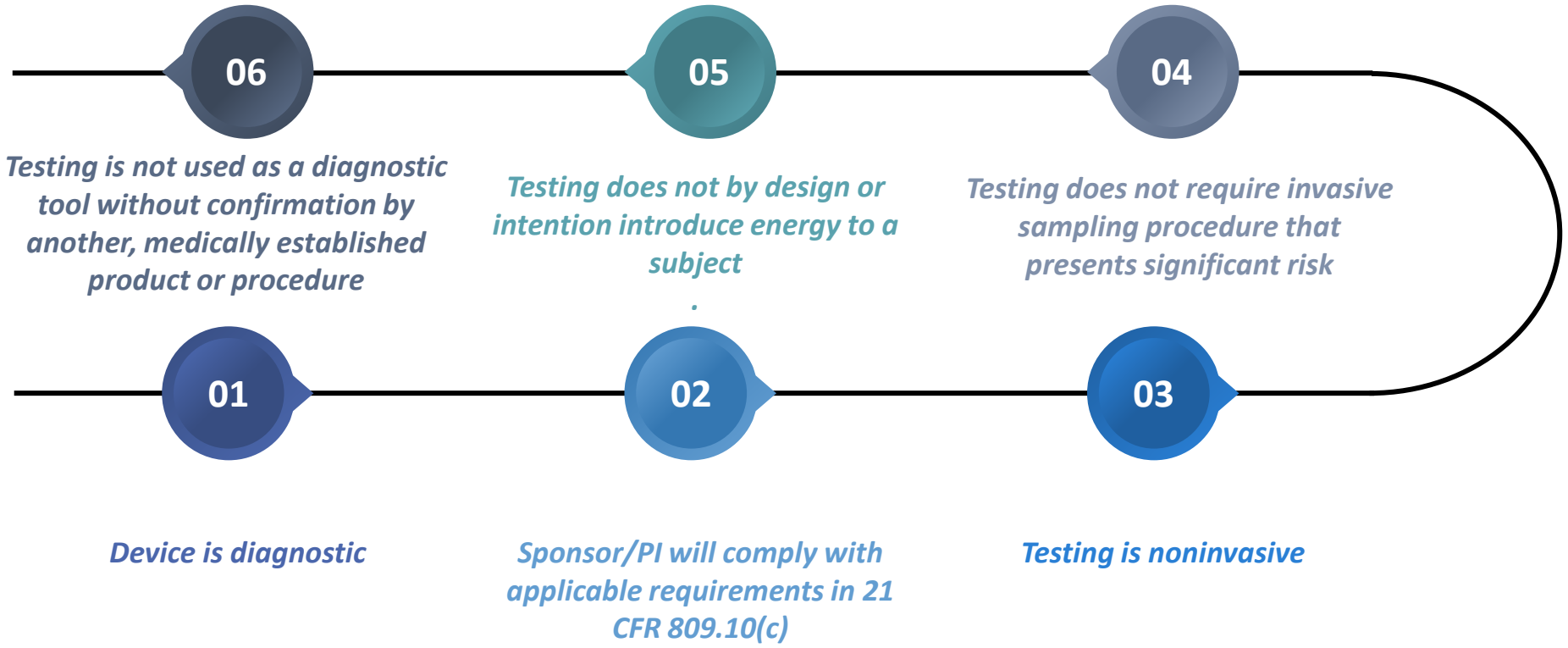
IDE Exemptions

IDE Exempt



Non-Significant Risk

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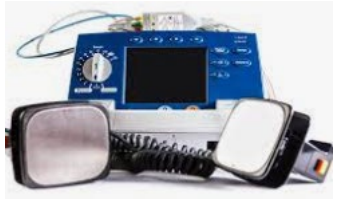
01 Not an Implant

*Is **not** intended as an implant **AND** does not present a potential for serious risk to the health, safety, or welfare of a subject*



Not Life Sustaining 02

*Is **not** purported or represented to be for use supporting or sustaining human life **AND** does not present a potential for serious risk to the health, safety, or welfare of a subject*

03 Not Diagnosing

*Is **not** for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health **AND** does not present a potential for serious risk to the health, safety, or welfare of a subject*

Not Serious Risk 04

Does not otherwise present a potential for serious risk to the health, safety, or welfare of a subject.

05 Justification

And that a justification is provided on how the above criteria be met including why the software should be considered as Non-significant risk.

Significant Risk

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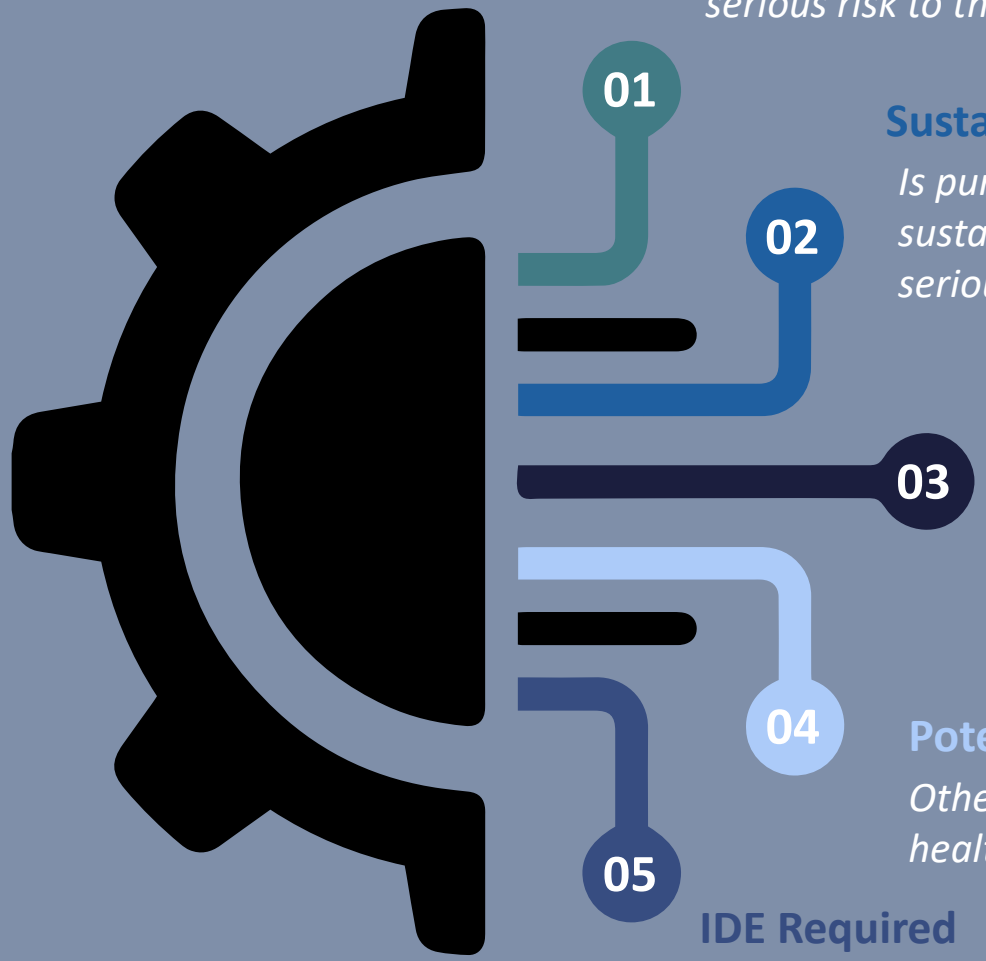

An Implant

Is intended as an implant AND presents a potential for serious risk to the health, safety, or welfare of a subject

Sustaining Human Life

Is purported or represented to be for use supporting or sustaining human life AND presents a potential for serious risk to the health, safety, or welfare of a subject

Used for Diagnosis

Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health AND presents a potential for serious risk to the health, safety, or welfare of a subject

Potential Serious Risk

Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

IDE Required

IDE is required from the FDA

Potential for Serious Risk

- Misdiagnosis
- Inaccurate result
- False positive

- Can result in psychological trauma from inaccurate or false result
- Can result in failure to initiate necessary treatment (e.g. sepsis, stroke, etc.)

Clinical Decision Support Tools

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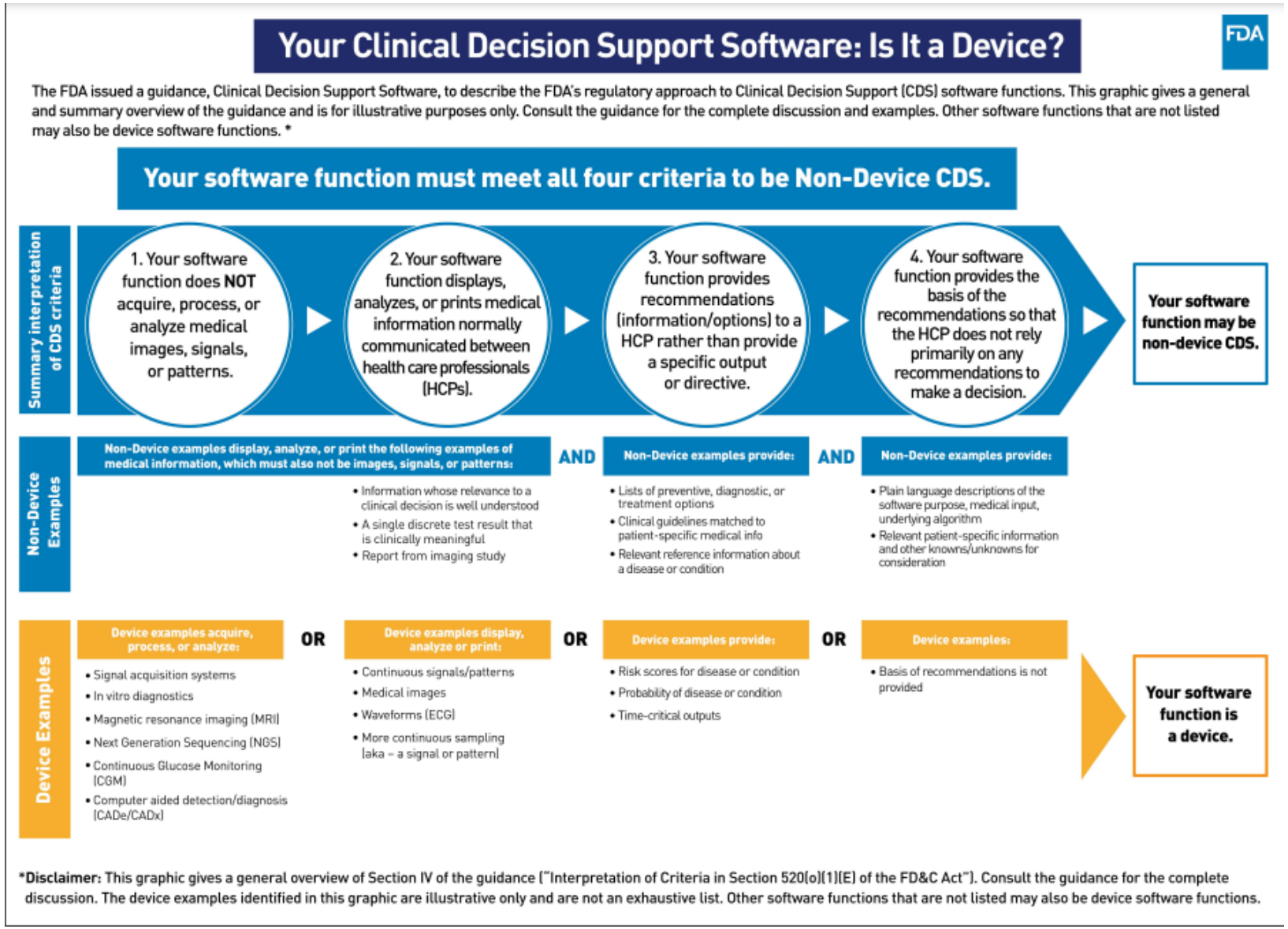

FDA Guidance: Your Clinical Decision Support Software: Is It a Medical Device?

FORM TS-AI
Research Involving Software

eIRB Tracking Number	STU

Complete this form if your study involves the development of a clinical decision support tool, machine learning, artificial learning, or predictive modeling. The IRB will use the information in this form, and other supporting documents, to determine if FDA regulations for medical devices are applicable for your study. If your study will involve the use of more than one software application (e.g., software, algorithm, predictive model, clinical decision support tool, etc.), please complete a separate form for each software application.

All clinical investigations of devices must have an approved IDE (or Non-Significant Risk Determination) or be exempt from the IDE regulations. Investigations that are exempted from 21 CFR 812 are described in §812.2(c) of the IDE regulations. Clinical Decision Support Software: Guidance for Industry and Food and Drug Administration Staff will also be considered. You may use Your Clinical Decision Support Software: Is It a Medical Device? (an FDA Decision tree) when filling out this form.

If more than one item will be utilized in this research study, complete a separate form for each item.

Software (e.g., Software, Algorithms, Predictive Model, Clinical Decision Support tool, etc.)

The following questions refer to the software, algorithm, model, or equivalent under evaluation.

1. Describe the software's current U.S. market status (FDA Approval)

☐	Approved or Cleared	☐	Unapproved

1.1 Describe the FDA approved/cleared software use and the specific method used to develop the software:

1.2 Are you using the software in accordance with the FDA approved indication?

☐ **Yes – Skip the remainder of this form and upload FDA approval/clearance information in the 6.17 Upload Other Documents**
☐ **No – continue**

1.3 Describe the investigational software and the specific method used to develop the software:

1.4 Who is developing the software *Enter Entity, UTSW/Affiliate Name, external collaborator, or vendor name here:*
Note additional institutional approvals may be necessary including but not limited to ISAC, OTD, etc.

1.5 Include a description of whether any regulatory determinations have been made by the FDA or if any preliminary risk assessments have been made.

2. Describe the current clinical workflow for evaluating the condition of interest.

3. Describe how diagnoses or treatment decisions are made under the current standard of care.

4. Who makes the diagnosis or final treatment decision?

☐ **Physician**
☐ **Nurse**
☐ **Advanced Practice Provider**
☐ **Other:**

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eIRB Tracking Number	STU

5. Describe the updated workflow in which the software will be used and include the following details:

a. **Who is the end user?**
b. **What is the output of the software determination?**
c. **What action is the user expected to take based on the software's output?**
d. **When the model is placed into the workflow what is the nature of the harm, if any, that may result from the use of the software?**

In your response, please indicate whether and how the use of the software may alter a clinician's approach to diagnosing, curing, mitigating, or treating disease. Indicate whether the clinician continues to make the determination of diagnosis and treatment of the condition with or without the use of the software.

6. Describe any additional tests/procedures individuals may need to undergo in order to validate the software.

7. Will the software acquire, process or analyze medical Images, signals, or patterns (such as x-ray, ultrasound, Sequencing, Continuous Glucose Monitors, Computer Aided Diagnostics, in vitro diagnostic device, etc.)?

☐ **Yes – The software is a medical device.**

☐ **No – Explain why the software does not meet this criterion:**

8. Will the software's function be limited to the display, analysis, or printing of medical information that is normally communicated between Health Care Providers (HCPs) about a patient or their medical information (such as symptoms, certain test results, discharge summaries, clinical practice guidelines, etc.)

☐ **Yes – Explain how the software meets this criterion:**

☐ **No – The software is a medical device.**

9. Will the software be limited to providing support or recommendations to the HCP about prevention, diagnosis, or treatment of a disease or condition to assist HCPs in making patient-specific decisions? (such as a list of preventive diagnostics, or treatment options)?

Note: If the software provides single or specific outputs (such as risk scores, probability of disease or condition), OR time-critical outputs (such as sepsis, stroke, or heart failure), or is intended to replace the HCP's judgment, it is a medical device-without other standard of care confirmatory procedures. Please address this issue in your response.

Note: if the software is intended to provide such recommendations to a patient or care giver (e.g., family member), it is a medical device. Please address this issue in your response.

☐ **Yes – Explain how the software meets this criterion:**

☐ **No – The software is a medical device.**

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FORM TS-AI
Research Involving Software

eIRB Tracking Number	STU

10. Will the software provide, in plain language, the basis of its recommendations via:

a. A description of the intended purpose or use of the product including the intended HCP user;
b. Identification of the required input medical information;
c. A description of the underlying algorithm development and validation including;
   i. A summary of the logic or methods e.g., AI/ML techniques;
   ii. A description of the data the model relied upon,
   iii. A description of the results from clinical validation studies; and
d. A description of the relevant patient-specific information and other knowns/unknowns for consideration?

☐ Yes – Explain how the HCP will be able to independently review the basis for the recommendations as outlined above. If the recommendations include (c)-(c-ii), as detailed above, please also explain how the HCP user is qualified to independently review this information. *Note: You may be requested to provide an example of the plain language recommendations to the IRB.*

☐ No – The software is a medical device.

11. Will the participant need to undergo an additional procedure as part of the investigational study resulting from the use of the software, for example, a surgical procedure or in additional procedures that are not driven by the clinician's determination?

☐ Yes – Describe additional procedures:

☐ No

12. Describe the process for handling missing or corrupted data.

13. Describe whether or not the software will be applied to patient groups whose data were not well represented in the development of the software.

14. How has the potential for algorithmic bias been evaluated and mitigated in the development of the software?

15. Describe additional security protocols in place to protect software from unintended access.

Upload this form to: 6.17 Upload Other Documents

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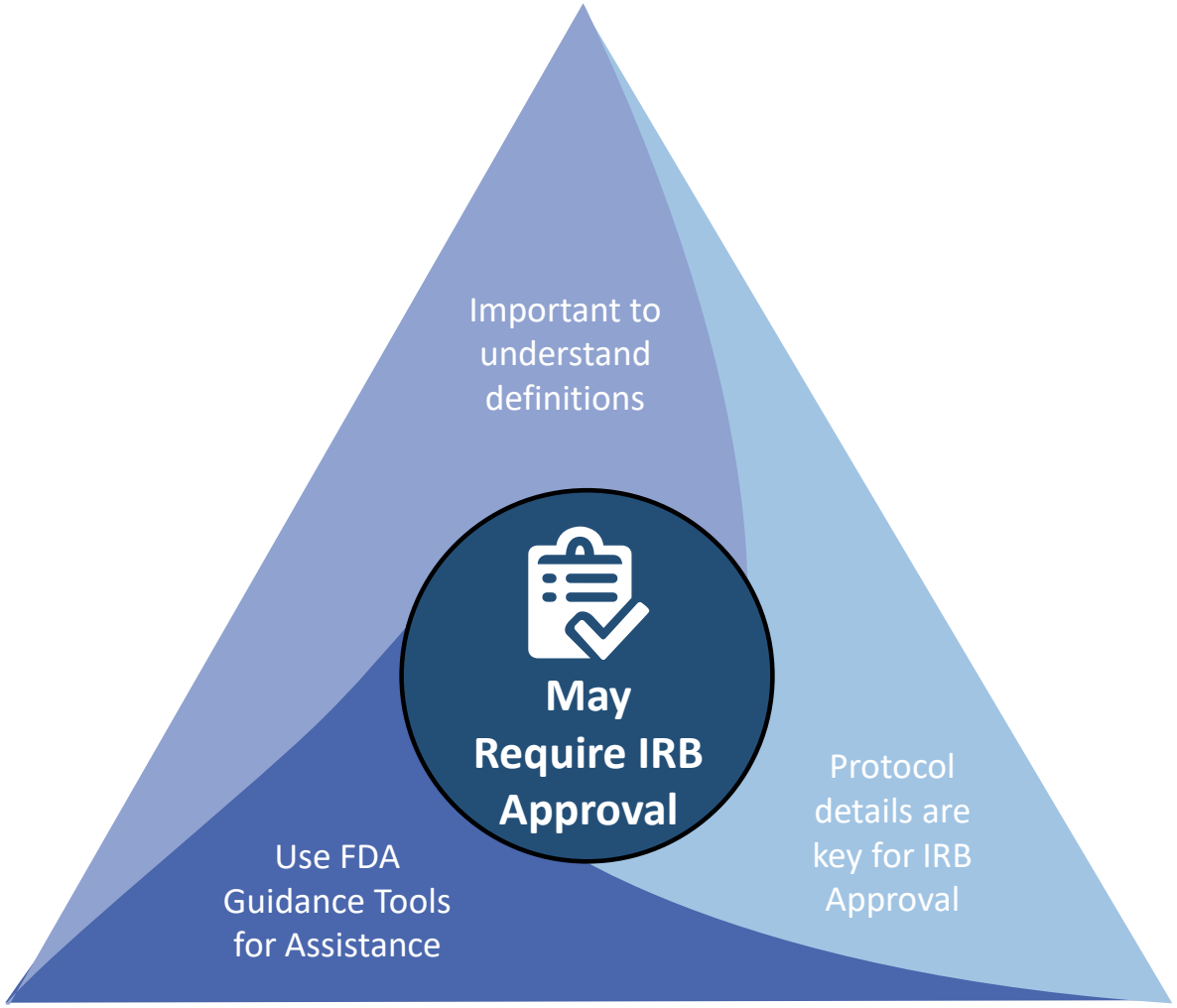
Summary


Important to understand definitions
May Require IRB Approval
Use FDA Guidance Tools for Assistance
Protocol details are key for IRB Approval

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References

- FDA
  - Artificial Intelligence and Machine Learning in Software as a Medical Device: https://www.fda.gov/medical-devices/software-medical-device-samd/artificial-intelligence-and-machine-learning-software-medical-device#whatis
  - Your Clinical Decision Support Software: Is It a Medical Device?: https://www.fda.gov/medical-devices/software-medical-device-samd/your-clinical-decision-support-software-it-medical-device
  - Step 1: Is the Software Function Intended For a Medical Purpose?: https://www.fda.gov/medical-devices/digital-health-center-excellence/step-1-software-function-intended-medical-purpose
  - Software as a Medical Device (SaMD): https://www.fda.gov/medical-devices/digital-health-center-excellence/software-medical-device-samd

- Presentation adapted from: 02/05/24 Webinar: Harmonizing Health and AI: Navigating Innovation and Ethics, presented by Tamiko Eto from Mayo Clinic

Thank You!

- **We'd love to hear your feedback.** We invite you to provide your evaluation of Research Matters and of the Human Research Protection Program.

- Visit: https://ais.swmed.edu/redcap/surveys/?s=3PRJFCFJJW