Artificial Intelligence Human Subjects Research (AI HSR)
IRB Reviewer Checklist

Reviewer:		**Date Received:**	
Principal Investigator (PI):		**Project ID Number:**	
Study Title:			

For "Research" involving Artificial Intelligence technology (e.g., AI/ML) and "Human Subjects", the IRB should review the IRB protocol in full, using standard reviewer checklist, ***in addition to*** the following AI Reviewer Checklist. **NOTE:** If technology is under investigation (evaluating efficacy and/or safety), ALSO use your institution's Investigational Device checklist.

Yes	No	N/A	AI HSR Determination, Protocol Checklist, and Other Considerations
I.			**Can this study be reviewed by your IRB? (Institutional Policy)** *Full Board and confirmation of acceptability from the Institutional Official documented.*
◯	◯		**Is the Study considered "Classified Research"?** If "yes", **STOP**. *Confirm with your legal department if permitted to conduct classified research.*
◯	◯		**Does the study involve "controversial" purposes?** **Examples**: *Military or lethal purposes; autonomous weaponry; subliminal techniques to manipulate a person's behavior; exploiting groups due to age, gender, sexuality, physical, or mental disability; social credit scoring; real-time remote biometric identification in publicly accessible spaces by law, etc.)*

II. Description of AI Technology (Note: List technology findings, version, etc. in approval letter)

☐ **Application lists the name of the technology and model(s)?**
☐ **Application defines status of the device**
Example: Model: *cmTriage, Version 3.1;* ***Developer:*** *Curemetrix;* ***Regulatory Status:*** *510(k)*

Health-Related? (check all that apply)	**Non-Health-Related? (check all that apply)**
☐ Clinical Use (intervention, Clinical or Patient Decision Support)	☐ Security
☐ Behavioral / therapeutic / Treatment	☐ Legal / regulatory
☐ Diagnostic	☐ Commercial / Marketing
☐ Preventative	☐ Improve academic performance
☐ Other: protocol should explain	☐ Participant Eligibility Determination
	☐ Other: protocol should explain

If technology is currently available (Check all that apply):	☐ Technology was developed in a separate project. Protocol should explain. ☐ Technology will be modified or will be used for purposes different from what it was originally designed, cleared, or approved for. ☐ Technology is currently legally marketed in the U.S. ☐ Technology is investigational but works as a component to a U.S. legally marketed device (ex: investigational AI/ML used with google glasses) ☐ N/A. Technology not currently available.

FOR MODEL DEVELOPMENT AND VALIDATION (if training, validating, or testing model):

◯ ◯ **METHODOLOGY: Does the technology have a transparent methodology? (Examples:** CRISP-DM, KDD, SEMMA, CPMAI, etc.)

Purpose of Technology (check all that apply):	☐ Prediction Model (Risk prediction, etc.)	☐ Mining text records
	☐ Automation	☐ Record abstraction
	☐ Biometric Recognition (face, voice, etc.)	☐ Other: protocol should explain
What kind of technology is being utilized? *(check all that apply)*	☐ Machine Learning (AI/ML)	☐ Deep Learning
	☐ Natural Language Processing (NLP)	☐ Unsupervised Learning
	☐ OTHER (Protocol should explain	☐ Reinforcement Learning

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IRB Reviewer Checklist

Algorithm adaptivity:	☐ Adaptive (learns in real time) ☐ Locked (doesn't change over time)

III. AI's Purpose in Study (check all applicable):	
What is the technology's CURRENT phase in this specific protocol application?	☐ **ONLY Proof of Concept (POC):** POC meant to illustrate a concept in a "almost real" environment but does not get deployed into real-world (includes training, validation, and testing) ☐ **Pilot:** Real-world project uses technology in protected environment but NOT for use in real-world production. ☐ **Real-world Pilot:** Interventions/treatment may run in parallel with the training and re-training of model.
☐	**ROLE of the AI (in meeting the aims of the study):** Confirm application describes the portion of the project that requires AI. Is the aim of the study entirely dependent upon the AI?
Is the technology *intended to* inform or to "drive" decisions? (medical or non-medical decisions. Ex: eligibility for a loan, or diagnosis or treatment determination)	☐ **"Inform":** decision made (and confirmed) without the technology, but the technology can support the decision. ☐ **"Drive"** intended for use as an autonomous diagnostic system. May alert physician or patient of identified risk.

IV. Does this study require IRB review?		
(1) Is this a clinical investigation, as defined by FDA? If "Yes", SKIP to Section V.		
◯	◯	*"Clinical investigation"* is synonymous with *"research". "Clinical investigation"* means any experiment that involves a test article and one or more human subjects, and that either must meet the requirements for prior submission to the FDA...or the results of which are intended to be later submitted to, or held for inspection by, the FDA as part of an application for a research or marketing permit.
AI Human Subject Research (AI HSR) Determinations (2 steps) **Note:** These questions should be in your IRB checklist. They may be described differently for AI. At least one (A or B) must be true.		
(2) Step 1: Is this "Research", as defined by the Common Rule? *Research is defined as a systematic investigation designed to develop or contribute to generalizable knowledge.*		
◯	◯	**(A) Is the project a "systematic investigation"?** ***1. Study has a recognizable study design*** *(randomized, grounded theory, product validation, etc.),* ***OR*** ***2. Study has a hypothesis, or research question****?* ***OR*** ***3.* Documents explain how study will determine project was successful.** ***Example:*** *We hypothesize our model has strong diagnostic accuracy and can identify cancers missed in clinical interpretation.* ***Example of study design that may NOT constitute a systematic investigation:*** ***QA/QI Example:*** Hospitals use AI to identify hospital admission rates and wait times in an emergency room, in order to improve overall performance and/or services.
◯	◯	**(B) Is the study designed to develop or contribute to generalizable knowledge?** ***For many sites, this question may be reframed as "technology or knowledge developed from this specific study can be made available for use outside of this immediate institution or department for future research or clinical use (even if provided at no cost)".*** (i.e., Will the results be generalizable to any situation beyond the situation being studied?) ***Example:*** Obtaining new understanding about humans (to model human behavior) or developing a new technology that can be used broadly to learn more about, model, or predict human behavior. ***Note:*** *Protocol should explain if the study is intended (wholly or partially) for the development of a product (even if provided will not be marketed).*
CONCLUSION: Is this project research? (2 "yes" responses needed) **If "No" to either question, STOP. NOT "research". If "Yes" to both questions, Continue.**		

Artificial Intelligence Human Subjects Research (AI HSR)
IRB Reviewer Checklist

Step 2: Does this "research" involve *"Human Subjects"*?		
◯	◯	**(A) Does the technology require *collecting or using* data (or specimens) *from or about* "living" individuals?** **Example:** Data is "human focused" and used to either model human behavior, OR help us understand human behavior or human health conditions. If "No", STOP. Not "human subjects"; If "Yes", continue.
◯	◯	**(B) Does the study involve obtaining identifiable information *about or from* individuals?** ***Identifiable information*** *includes information about living individuals where the identity of the subject is identified or may be identified* ***(or generated)*** *by the investigator or a third-party in a reasonable amount of time through reasonable efforts.* **Note:** Limited Datasets containing health information are considered PHI and identifiable. If "No", STOP. Not "human subjects"; If "Yes", Continue.
◯	◯	**(C) Does the study involve obtaining PRIVATE information or Protected Health Information (PHI) about living individuals?** ***Private information*** *includes information about living individuals' behavior,* ***occurring in*** *a context with a reasonable expectation of privacy (e.g., activities in one's home or classroom), or information provided with a reasonable expectation of privacy (e.g., medical records, school grades, personal posts or messages on social media or any other website where membership or special passwords/access privileges are required).* If "No", STOP. Not "human subjects"; If "Yes", Continue.
If one "Yes" above, are there interactions or interventions?		
◯	◯	**Does the study involve any *interactions*** (communication, virtual, directly or indirectly; Ex: email, opt-in/opt-out, sending flyers, and/or via robots)? **If "Yes", protocol should describe AI's role in the interaction.** ***Example:*** ***Direct:*** *person engages with AI model;* ***Indirect:*** *person's data is used by the model ONLY.*
◯	◯	**Does the study involve any *interventions*?** (Includes procedures by which technology is used as a means of collecting data to manipulate, manage, or influence a person, their environment or condition, including advising on a course of action as a result of the AI output? ***Example 1:*** *Participants wear sensor, scanned by device, or perform tasks to obtain physiological measurements, or biometric identifiers.* ***Example 2:*** *Prediction Model identifies someone at risk; informs physician who would then alter treatment based on output/recommendations.*
CONCLUSION: The project is "Research" that involves "Human Subjects". Continue.		

V.		**FDA: Is the technology *possibly* regulated by FDA?** If No, **SKIP to Section VI.**
◯	◯	**Does this device meet the** definition of Medical Device**?** *"…intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals…"*
◯	◯	**SaMD** (Software *as* a Medical Device)? The software/AI/ML may be used in a medical device, but the medical device does not rely on the software to function.
◯	◯	**SiMD** (Software *in* a Medical Device)? Hardware/machine/device depends on AI to function (for example, AI helps to run a medical device; or AI is the primary way to view output)
Is the AI an investigational device? (Note: these are still subject to 21 CFR 50 & 56)		
◯	◯	Has this AI been cleared or approved by FDA for the same purpose as in this study?
◯	◯	Will any data need to be held for inspection by the FDA either now or later?
◯	◯	Is this technology exempt from the IDE requirements? (21 CFR 812.2(c))

		Example: a diagnostic technology that meets all 4 criteria, 510(k) used as labeled, consumer preference testing, or testing of a combination of two or more U.S. legally marketed devices) **If 510(k),** provide #: **Example: K123456**
◯	◯	**If the device study is NOT exempt from IDE?** If yes, technology requires the IRB to make an SR/NSR determination. Refer to your institution's SR/NSR SoP.
☐		Confirm information is included about the risks of the device as used in this study.

VI. Additional Ethical Considerations	
A) Respect for Persons:	
	1. Data Integrity:
☐	**Transparency:** *(i)* Confirm the source and characteristics of data used to train the model are clearly explained (e.g., What datasets are going to be utilized? Will datasets be combined and why?) *(ii)* If applicable, confirm application and Informed Consent Form describe how participants will be notified when an AI product is part of their care or wellbeing, and what data that was trained on. **Note:** *If Participants will not be notified, strong justification is provided.*
☐	***Un-Blackboxing:*** Confirm protocol describes how the model(s) function; the process and role of the model's output in final decision-making are explained ***and*** (if consent is required) comprehensible to the participants (e.g., is the "black box" addressed?).
☐	**Data Source:** Protocol describes method and sources of data collection (Example: Application Programming Interface (API); scraping (automated programs to collect data, faces, voices, etc. from a website in a methodical way, including URLs) to provide access to the data of an application or operating system)
☐	**Data Disposition:** Confirm application describes what will happen to the data when this specific project is complete. **Example:** Will the model continue using the data for future training? Will the model be shared? With whom?
	2. Explainability (Human interpretability): *Confirm protocol is written so researcher can examine the input features that were most important in making the decisions it made.*
☐	Describes how they are using the best available interpretability technology.
☐	Confirm commitment to updating model as technology improves.
☐	**Training and Monitoring:** Application describes continuous training/iteration and monitoring of model (to account for data change, or model drift over time)**. Note:** ***(i)*** Model training should be done with prospective data collection. ***(ii)*** If no re-training, protocol should explain why.
B) Justice*: No group bears the burden of testing (or being the test of) new technologies while other groups reap the rewards*	
☐	**Representativeness:** Confirm the diversity in the **data source** meets the needs of the study design and procedures (including recruitment) to ensure equitable selection. Consider race, skin tone, gender, disability, etc.
☐	**Minimize Disparities:** Protocol describes how algorithmic decisions do not create discriminatory or unjust impacts, such as health disparities, when comparing data across different demographics or affected communities and individuals. **Example:** Technology generalizable to groups outside those the model was trained on; Ensuring external validation and model re-calibration prior to implementing in real-world or clinical workflow.
☐	**Secondary Participants/Incidental Participant:** Describes what features of data will be used in the final model. ***Example:*** *a project focuses on broader populations (group) characteristics or environment, but to do so, individual measurable properties and/or characteristics of a phenomenon being observed contain potential PII/PHI such as age, gender, height, weight, gait, voice or facial recognition, etc.). Project collects data on each individual so that the AI can learn how to single out "noise" or "silence" outside data.*
C) Beneficence: Do no harm; minimize harm; maximize benefit. To adequately assess the risk-to-benefit ratio ***in uncertain and non-transparent AI***, and confirm the risks of participation do not outweigh the potential benefits of participating in the study, consider the following:	
☐	Describes who will directly benefit from this technology. Describes how findings and general knowledge benefit the populations of which the data originates. **Note:** If the benefit is limited to a specific population or setting, justification is required.

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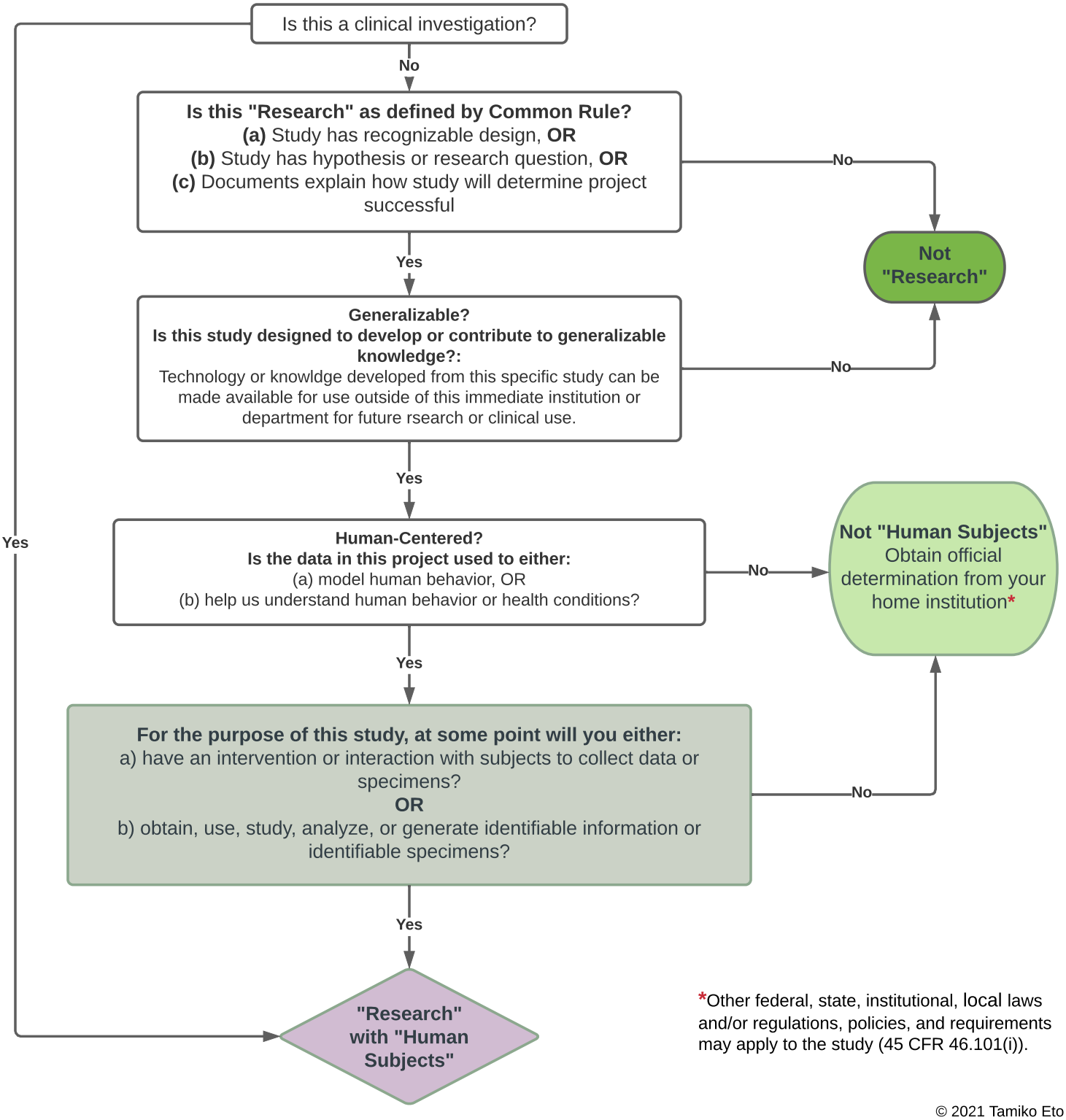
IRB Reviewer Checklist

(C)(1) Monitoring Plan / Risk Mitigation: Confirm plan for monitoring how the AI is being used is clearly described.	
☐	***What could go wrong?*** Describes what possible mistakes it could make, be abused, or cause harm to others (e.g., nefarious use, dual use, incrimination of illegal activities, bias in algorithm, etc.)
☐	Describes possible risk(s) if any action or output is acted on autonomously, especially if such action might affect a human's health or wellbeing.
☐	Describes adequate controls in place for preventing abuse during the research, and after the research is complete.
☐	Describes iteration requirements and plans for continuous monitoring and evaluation of the data (retraining model); if not needed, PI must explain why. **Example:** the real-world environment doesn't change.

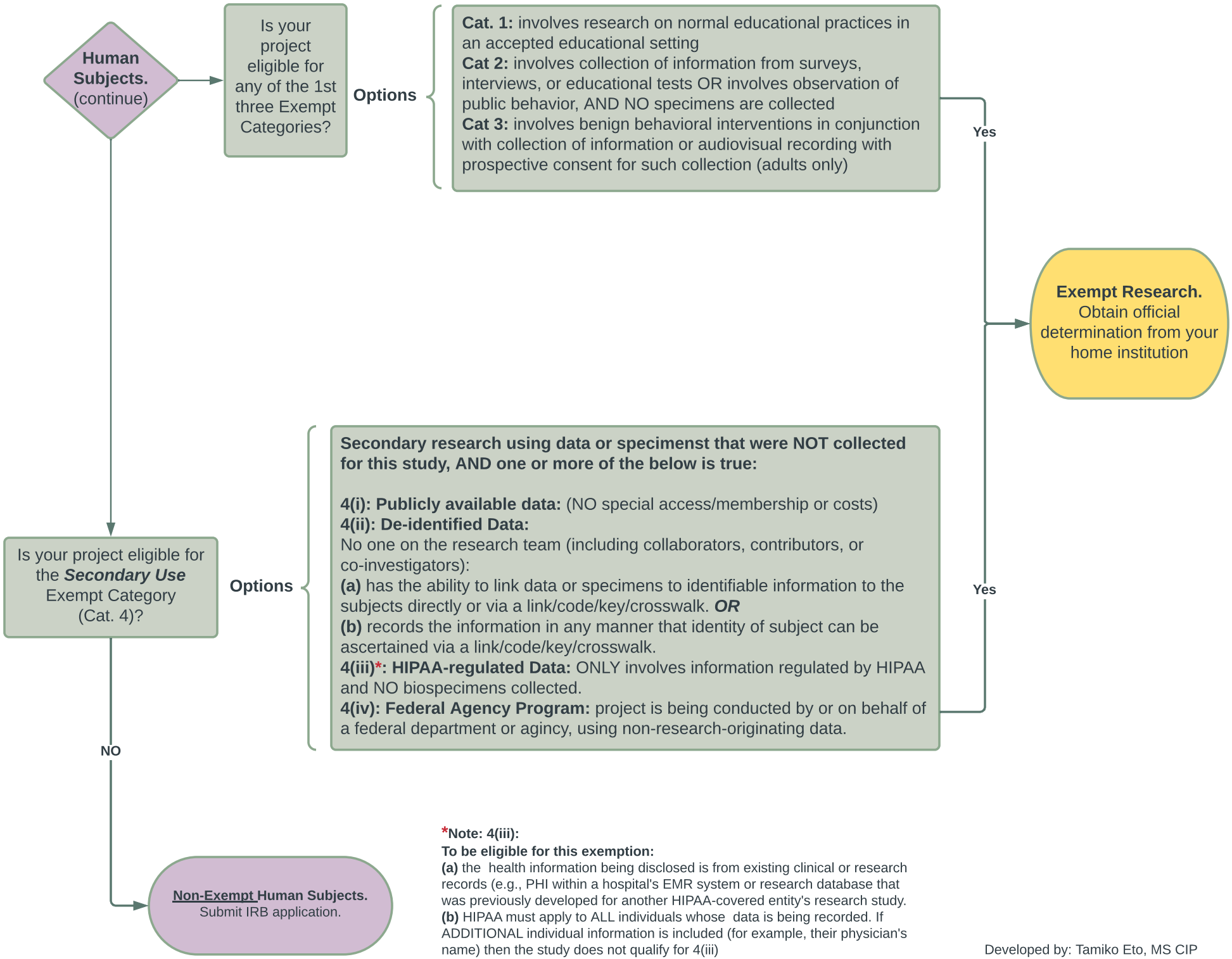
VII. Privacy & Confidentiality (45 CFR 46.111(a)(7); 21 CFR 56.111(a)(7))			
(A) Privacy: **AI-specific concerns about data use:** To what extent do the subjects have control over the circumstance around sharing oneself (and/or their data/information) with others?			
☐			**Privacy Limitations addressed?** Consent (if required), ***and*** application clearly explain limitations of privacy and confidentiality (e.g., due to utilization of external vendor services such as Google, Amazon, etc.)
☐			**Privacy Concerns addressed?** PI and IRB should consider if the subject would want this information kept private. Would they be surprised or unhappy if they found out you were using it?
(B) Data Collection & Maintenance			
◯	◯	◯	**3rd Party Data Collection or Storage?** Data use and Terms of Use/Service (ToU/ToS) requirements of third-party sources such as Facebook, Instagram, Twitter, dating websites, YouTube, LinkedIn, other social media websites, etc. have been reviewed by PI and provided to IRB for review.
◯	◯	◯	**Merging Datasets:** Consent (if applicable) ***and*** IRB application describe **(i)** if (and how) participant's data will be combined with other datasets, **(ii)** the possibility of re-identification and/or obtaining additional information, **(iii)** why this information is needed, and (**(iv)** name of additional data source(s).
☐			**Data Minimization:** Justification for each datapoint is included: only includes the bare minimum necessary in order to meet the study's purpose (absolutely necessary, and that the study goals could not practicably be achieved without that specific data).
(C) AI-specific Confidentiality Considerations: Does the researcher's plan include specific considerations for future data usage in iterative training models.			
☐			Consent (if applicable) ***and*** application describe how participant's audio/visual/biometric (voice, finger, facial, retina scans, etc.) data is used, stored (coded, transposed, etc.), shared, destroyed/not destroyed, de-identified/not de-identified, etc. ***during*** and ***after*** this specific project ends?
☐			Describes any reasonably foreseeable purposes in which participant data may be used in the future, how it will be shared, with whom it will be shared, how long it will be stored, when it will be destroyed.
◯	◯	◯	***Biometric datapoints used to determine eligibility?*** i.e., for, or access to a program, service, or opportunity, consent form (if applicable). Confirm IRB application describes those.

VIII. Misc. Considerations		
◯	◯	**Future Modifications Considerations:** Can the protocol be designed broad enough so that model changes can fit within the approved scope of the study? ***Example 1:*** *Allowing modifications to algorithm/device so long as the general procedures and design of study are not altered, and risks do not increase.*
◯	◯	***Accountability:*** Confirm protocol describes how technology is designed and implemented in publicly accountable ways, such as an obligation to report; explains and justifies specific decisions, mitigates negative impacts and potential harms.

Aritificial Intelligence Human Subjects Research
(AI HSR) Determination Decision Tree
(to be used for AI/ML HSR Determinations)



*Other federal, state, institutional, local laws and/or regulations, policies, and requirements may apply to the study (45 CFR 46.101(i)).



***Note: 4(iii):**
To be eligible for this exemption:
(a) the health information being disclosed is from existing clinical or research records (e.g., PHI within a hospital's EMR system or research database that was previously developed for another HIPAA-covered entity's research study.
(b) HIPAA must apply to ALL individuals whose data is being recorded. If ADDITIONAL individual information is included (for example, their physician's name) then the study does not qualify for 4(iii)
(c) data cannot be shared with a non-HIPAA covered entity

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