University of California San Francisco

INVESTIGATOR CHECKLIST FOR: IDE Exempt, Non-Significant Risk, or Significant Risk Device Studies

The purpose of this checklist is to help investigators and the IRB determine whether a clinical investigation designed to determine the safety or effectiveness of a device is IDE Exempt, Non-Significant Risk, or presents Significant Risk.

Note: Determinations of IDE Exempt, Non-Significant Risk, or Significant Risk are needed only for devices that meet the FDA's definition of a medical device,[i] which is "an instrument, apparatus, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is:

- recognized in the official National Formulary, or the United States Pharmacopoeia, or any supplement to them,
- 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, or
- intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes."

Device Name & Manufacturer:	IRB#:	Principal Investigator:

Instructions: Start with Section A. If you are unsure whether the criteria are met, complete Section B. If not met, continue to Section C.

Include this completed checklist in the Other Study Documents section of your iRIS submission to the IRB, and any correspondence from the FDA and/or study sponsor regarding the device. *Complete one Checklist for each device*.

For consultations regarding medical devices, including help determining whether your device meets the FDA definition of a medical device, see FDA Regulatory Support at UCSF or e-mail: FDAconsults@ucsf.edu.

A. IDE EXEMPT DEVICE STUDY. Check if Yes.

All criteria under at least one category must be Yes for the device to be exempt from the IDE requirement. If none of the categories for exemption apply (or if unsure), complete Section B.

Category #1	☐	**Older Devices** (this category is rarely used): A device in commercial distribution (legally marketed in the U.S.) immediately before May 28, 1976, when used or investigated in accordance with the indications in the labeling that were in effect at that time.
Category #2	☐	**Substantial Equivalence (510(k) clearance):** A device introduced into commercial distribution (legally marketed in the U.S.) on or after May 28, 1976, that the FDA has determined to be substantially equivalent (see 510(k) clearance database[ii]) to a device in commercial distribution and that is used or investigated in accordance with the indications in the labeling FDA reviewed in determining substantial equivalence.
Category #3		The device is a **diagnostic device**[iii] (*e.g.*, in vitro diagnostics (IVDs), testing assays, laboratory developed tests (LDTs), and genomic sequencing):
	☐	The testing is **noninvasive**[iv].
	☐	The testing does not require an **invasive sampling procedure**[v] that presents significant risk.
	☐	The testing does not by design or intention **introduce energy** into a subject.
	☐	The testing is not used as a diagnostic procedure without **confirmation**[vi] by another, medically established product or procedure.
	☐	The sponsor will comply with applicable (**labeling**) requirements in 21 CFR 809.10[vii].
Category #4	☐	The device is undergoing **consumer preference** testing, testing of a **modification**, or testing of a **combination** of two or more devices in commercial distribution (legally marketed in the U.S.), and the testing is **not for the purpose of determining safety or effectiveness** and does not put subjects at **risk**.

Note: Categories 5 and 6 of Exempted Investigations (21 CFR 812.2) do not apply to human research and are therefore omitted here.

Category #7	☐	The device is a **custom device**[viii], unless the device is being used to determine safety or effectiveness for commercial distribution.

If the criteria for one of the above exempt categories are met, STOP here. **Include the rationale for exemption** below. If none of the categories is met, or if you are unsure about exemption, continue to Section B.

Protocol-specific rationale for why the device meets the above IDE Exempt criteria:

University of California San Francisco

INVESTIGATOR CHECKLIST FOR: IDE Exempt, Non-Significant Risk, or Significant Risk Device Studies		
Version	DATE	PAGE
6	10/09/18	2 of 2

B. NON-SIGNIFICANT RISK (NSR)[ix] DEVICE STUDY = ABBREVIATED IDE. Check if Yes.

☐ Non-Significant Risk Device: meets none of the criteria below for C. Significant Risk Device.

Protocol-specific rationale for why the device does NOT meet any of the Significant Risk criteria (refer to Section C criteria):

If none of the Significant Risk Device Study criteria are met, the IRB can make the NSR determination. If the IRB finds the study is NSR, the device is considered to have an Abbreviated IDE (21 CFR 812.2(b)). If the IRB disagrees and finds Significant Risk, an IDE application to FDA is required. Include documentation of the IDE in the Other Study Documents section of your iRIS submission to the IRB.

C. SIGNIFICANT RISK DEVICE STUDY. Check if Yes. If the IRB or FDA agree the study is significant risk, an IDE application to FDA is required. Include documentation of the IDE in the Other Study Documents section of your iRIS submission to the IRB.

☐ Is intended as an implant[x] and presents a potential for serious risk to the health, safety, or welfare of a subject.

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

☐ 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.

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

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[i] Medical device definition: https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/Overview/ClassifyYourDevice/ucm051512.htm

[ii] Searchable 510(k) database: https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm

[iii] For diagnostic devices, even if a test is validated for CLIA purposes, the FDA issues are evaluated separately.

[iv] 21 CFR 812.3 (k) *Noninvasive*, when applied to a diagnostic device or procedure, means one that does not by design or intention: (1) Penetrate or pierce the skin or mucous membranes of the body, the ocular cavity, or the urethra, or (2) enter the ear beyond the external auditory canal, the nose beyond the nares, the mouth beyond the pharynx, the anal canal beyond the rectum, or the vagina beyond the cervical os. For purposes of this part, blood sampling that involves simple venipuncture is considered noninvasive, and the use of surplus samples of body fluids or tissues that are left over from samples taken for noninvestigational purposes is also considered noninvasive. 21 CFR 812.3(k)

[v] In Vitro Diagnostic (IVD) Device Studies -Frequently Asked Questions: To determine whether an **invasive sampling technique** presents a serious risk, we recommend that you base your risk determination on the nature of the harm that may result from sampling. For example, FDA considers sampling techniques that require biopsy of a major organ, use of general anesthesia, or placement of a blood access line into an artery or large vein (subclavian, femoral, or iliac) to present a significant risk.

[vi] In Vitro Diagnostic (IVD) Device Studies -Frequently Asked Questions: To be exempt under 21 CFR 812.2(c)(3), clinical investigators must use a **medically established** means of diagnosis (e.g., another cleared or approved IVD or culture) of the disease or condition **as the basis for decisions regarding treatment** of all subjects participating in the study. 21 CFR 812.2(c)(3)(iv). Additionally, test results from the exempt IVD investigation **should not influence patient treatment or clinical management decisions** before the diagnosis is established by a medically established product or procedure.
If an investigational test uses a new technology or represents a significant technological advance, **established diagnostic products or procedures may not be adequate to confirm the diagnosis** provided by the investigational IVD. For example, if an investigational test is designed to identify an infection at the earliest stages of viral infection (before formation of antibodies), established diagnostic products or procedures that rely on the detection of antibodies to the virus would be inadequate to confirm diagnoses. Under these conditions the study would not meet the criteria for exemption under 812.2(c)(3) since the testing could not be confirmed with a medically established diagnostic product or procedure. You may consider whether the device is a non-significant risk device subject to abbreviated IDE requirements (21 CFR 812.2(b)).

[vii] 21 CFR 809.10 Labeling for in vitro diagnostic products.

[viii] To be considered a **custom device**, all of the criteria at section 520(b) of the Federal Food, Drug, and Cosmetic Act must be met, which are summarized below:
(1) It necessarily deviates from devices generally available or from an applicable performance standard or premarket approval requirement in order to comply with the order of an individual physician or dentist;
(2) The device is not generally available to, or generally used by, other physicians or dentists;
(3) It is not generally available in finished form for purchase or for dispensing upon prescription;
(4) It is not offered for commercial distribution through labeling or advertising; and
(5) It is intended for use by an individual patient named in the order form of a physician or dentist, and is to be made in a specific form for that patient, or is intended to meet the special needs of the physician or dentist in the course of professional practice (such as a particular operating tool).

[ix] See UCSF Guidance on Significant vs. Non-Significant Devices and/or FDA Information Sheet Guidance on Significant and Non-Significant Risk Medical Device Studies for additional information and examples.

[x] An **implant** is a device that is placed into a surgically or naturally formed cavity of the human body and is intended to remain there for a period of 30 days or more. In order to protect public health, FDA may determine that devices placed in subjects for shorter periods are also implants.
https://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046698.htm An **implant** is a device that is placed into a surgically or naturally formed cavity of the human body and is intended to remain there for a period of 30 days or more. In order to protect public health, FDA may determine that devices placed in subjects for shorter periods are also implants.
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