

Guidance for In Vitro Diagnostic Device Studies

About IVDs

In vitro diagnostics (IVD) are tests that can detect diseases, conditions, or infections. Some tests are used in laboratory or other health professional settings and other tests are for consumers to use at home. IVD devices include products used to collect specimens, or to prepare or examine specimens (e.g., blood, serum, urine, spinal fluid, tissue samples) after they are removed from the human body. This would include a genetic testing device intended for use in the diagnosis of diseases or other conditions.

Purpose of this Guidance

The purpose of this guidance is to explain the regulatory requirements of in vitro diagnostic (IVD) device studies - including IRB review and consent requirements for IVD diagnostic device studies **using leftover specimens**. This information comes from FDA guidance issued in June 25, 2010, referenced in the footnote of this document, along with FDA guidance issued April 25, 2006. We will heavily rely on the FDA guidance's language in this document.

Regulatory Requirements for IVD device studiesⁱ

Is an Investigational Device Exemption (IDE) required for IVD device studies?

Some IVD device studies are exempt from IDE regulations (21 CFR Part 812). In order to be exempt for the IDE regulations, an IVD study must fit in one of these three categories:

1. The IVD is a pre-amendments device (i.e., a device that was in commercial distribution prior to the enactment of the 1976 Medical Device Amendments to the Act), other than a transitional device, and is used or investigated according to the indications in the labeling at that time.
2. The IVD is a device, other than a transitional device, that has been found to be substantially equivalent to a pre-amendments device and is used or investigated according to the indications in the labeling reviewed by FDA in determining substantial equivalence.
3. The IVD:
 - a) Is properly labeled in accordance with 21 CFR 809.10(c)
 - b) Is noninvasive
 - c) Does not require an invasive sampling procedure that presents significant risk
 - d) Does not by design or intention introduce energy into a subject
 - e) Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure

If the study does not fit in any of these categories, the sponsor needs to seek an IDE.

Please refer to the FDA guidance for more information about when a device presents significant risk and what they mean when they say “confirmation of the diagnosis by another, medically established diagnostic product or procedure.”

Is an IVD study considered human subjects research?

Under the FDA’s definition of “subject,” a subject would include individuals whose specimens are tested with an IVD [21 CFR 812.3(p)]. So, even if there are **no** identifiers on the specimens, the research would involve “human subjects” per the FDA’s definition, and therefore require IRB review and adherence to the FDA’s regulations for clinical investigations. (This is in contrast to non-FDA-regulated studies, where use of anonymous specimens or data would not be considered “human subjects” research.)

Can investigational IVD studies receive expedited IRB review?

Yes, as long as they are minimal risk (as determined by the IRB) and fall into one or more categories defined in the regulations (see 21 CFR 56.110). Note: A study may not be expedited if identification of the subjects and/or their information would reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, insurability, reputation, or be stigmatizing, unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal. Thus the type of diagnosis may impact whether the study is deemed “minimal risk.” (63 FR 60353, November 9, 1998).

What if my study uses only *completely de-identified* leftover specimens?ⁱⁱ

Then, per FDA regulations, the study will still fall under the FDA device and human subjects’ research regulations, and must be reviewed by an IRB. The FDA’s definition of human subject includes individuals on whose specimens an investigational device is used.ⁱ Note that the requirement for informed consent therefore applies to the study; however, FDA has agreed to exercise “enforcement discretion” in these cases, as described in the next section.

In order for the IRB to evaluate whether the study meets the enforcement discretion criteria, please fill out the [Waiver of Consent for *In Vitro* Diagnostic Device](#) worksheet.

When would informed consent from subjects be required, if using leftover specimens?

An IVD study using leftover specimens **will** need to obtain informed consent from subjects if any of the following applies:

1. Study is using **identifiable** leftover human specimens, meaning that the sample can be linked to the subject (even if just by a random code)
2. The study does not meet the IDE exemption criteria at [21 CFR 812.2\(c\)\(3\)](#), listed above.
3. The specimens were collected specifically for the proposed investigation. That is, the specimens are not leftover from routine clinical care or analysis, or leftover from other research
4. The amount of specimen needed for the study is more than would be left over from what is usually collected for routine clinical analysis, or

5. The test results will be reported to the subject's health care provider. For example, in the course of comparative studies involving B. anthracis detection devices, it would be inappropriate to not report positive results if they occur in the course of an investigation.⁽ⁱ⁾ (Of course, this implies that the specimens are identifiable as well, so (1) would have already made consent required)

What would constitute a de-identified leftover specimen?

A de-identified leftover specimen is one that does not have any identifier (name, medical record number, date, code, etc.) that the researcher(s) could use to link the sample with the patient. If the sample is de-identified with a code, make sure that neither you nor any other investigators on the study have or had access to a key that could link any code to an individual. For the purposes of this document, coded means that: 1) a number, letter, symbol, or combination thereof (i.e., the code) has replaced identifying information (such as name or social security number) that would enable the investigator or any other individuals associated with the investigation, including the sponsor to readily ascertain the identity of the individual to whom the specimen pertains; and 2) a key to decipher the code exists, enabling linkage of the identifying information to the specimen.⁽ⁱ⁾

Who should I contact if I have additional questions?

You may contact the [IRB Education and QA team](#) at (404) 712-0724, or the Office of Compliance at orc@emory.edu or at (404) 727-2398.

ⁱ FDA Guidance: [In Vitro Diagnostic \(IVD\) Device Studies -Frequently Asked Questions](#)

ⁱⁱ FDA Guidance [on Informed Consent for In Vitro Diagnostic Device Studies Using Leftover Human Specimens that are Not Individually Identifiable](#)