

INFORMATION about Research with “Unidentified” “Waste” Specimen

In an oddity of regulation, the device regulations found in 812.3 define a human subject as a person “on whose specimen” a study is done. A study with human subjects requires IRB review.

IRB review is governed by 21 CFR Part 56. Part 56 requires the IRB to assess the informed consent process and documentation. *FDA allows very few waivers of consent and none that apply to use of waste specimens.* Thus, the IRB should require consent from the original (presumably anonymous) donor.

FDA’s guidance of April 25, 2006 recognized that obtaining informed consent from the unidentified donor of a left-over specimen is difficult and that, while consent cannot be waived, they will use their “enforcement discretion” in inspections of device studies regarding the issue of informed consent. This shifted the burden to the IRB to decide how much discretion to use.

To do its job, the IRB needs sufficient information to determine that the required review elements can be met. This form should accompany a protocol for the acquisition and use of the specimen. We do NOT want a laboratory protocol.

A. THE INVESTIGATOR	
A.1. Who are you and where are you?	What is your role in this project?
Name (with degrees)	<p>What is the intended start date</p> <p>A few days is required but a few weeks decreases everyone’s stress levels.</p>
Company	
Mailing address	
City, State, Zip	
Phone	
Fax	
e-mail	
Attach <input type="checkbox"/> your resume and <input type="checkbox"/> a description of the company and its url	

An investigator is the person controlling the study. This should be the person who authority over the acquisition phase which is of interest to the IRB.

A. THE ACQUISITION SOURCE	
A.1. Who is the responsible person at the source?	Describe the type of site involved? (e.g. central laboratory, private practice, hospital, bank or repository, etc.)
Name (with degrees)	<p>Some places such as teaching hospitals have tight controls and consent requirements that we can count on while some have no controls. The more you can find out about their policies, the better.</p> <p>It is hard to have a research subject without research. This question presumes that the activity is either “research” or a “clinical investigation”.</p>
Company	
Mailing address	
City, State, Zip	
Phone	
Fax	
e-mail	
Attach <input type="checkbox"/> a description of the cooperating site and its url.	

B. IS THERE REALLY A HUMAN SUBJECT?
 If there is no human subject, no IRB review is required.

1	Is there any direct intervention FOR THE STUDY to obtain the sample?	<input type="checkbox"/> Yes <input type="checkbox"/> No	If there are 4 NO responses, there are no human subjects.
2	Is there any direct interaction FOR THE STUDY to obtain the sample?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
3	Is there any code or information that could be used to link back to a specific individual?	<input type="checkbox"/> Yes <input type="checkbox"/> No	If there is 1 yes, IRB review is necessary.
4	FDA: Is an in vitro diagnostic device to be tested using a human specimen?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
			If yes, there is human subject research which requires IRB review

C. REVIEW OF THE STUDY

C.1. Under 21 CFR Part 56, an IRB must make a series of determinations. The following will provide the information to make those decisions.

1.	Describe the purpose of this study. Why is it being done? What is the probable benefit from a positive outcome?		56 is about IRB review including risk/benefit, equitable selection, and informed consent.
2.	Describe the study design. Are you using the fewest samples to accomplish the goal?		
3.	Describe the procedures. <ul style="list-style-type: none"> ▪ What is being acquired? Type of specimens, quantity, ▪ Your source: Federal or private repository, colleague, clinical laboratory, pathology ▪ Original source: where did your source get the specimens? 		The IRB is interested in the donor person rather than the lab procedures. The "protocol" should be about HOW the human subject/donor is (or is not) involved.
4.	Agreements: Did the agreement with your source cover ethical acquisition, identifiers, consent, and destruction? Did you make clear the intended use?		
5.	What are the risks to the original donors? (consider emotional or social factors). <ul style="list-style-type: none"> ▪ Is there any possibility of emotional or social risk to the racial/social or ethnic group of the donor? ▪ Is the intended use foreign to or related to the donor's condition? 		<ul style="list-style-type: none"> • A donor is unaware of a donation but is contacted for infectious disease testing following a lab accident. • An unusual condition is being studied and patients want to keep their patent position clear. • Use your imagination.
6.	Confidentiality and De-Identification Process <ul style="list-style-type: none"> ▪ Was the sample ever identifiable? ▪ When it left the original provider, what identifiers or code was used? ▪ When it got to you, what information was available? ▪ What firewall is there between your source and you? ▪ Is it possible, if absolutely necessary, ever get information back to the donor or the donors physician? 		In the most urgent case, would it ever be possible for anyone to work back to find the identity of the original person? Too often submissions say it is "de-identified" without any explanation. HOW does the sample move from patient identity to without any link?
7.	What criteria are used to select (requisition) samples? Are there any issues concerning equitable selection or bias?		

8 Given the size of the population being studied, is there any chance that a small group of people could be identifiable?	This is just cell size.
9. Are the samples from a population that might be considered vulnerable such as children, employees, or those with decision-making issues.	
10 Was informed consent for research use been gained? Please explain as much as you possibly can. (e.g., leftovers from a clinical trial with specific consent)	If consent was gained - excellent. The FDA discretionary waiver of consent is not needed. If not, C.2 is essential.
11 Was that consent documented? If possible, please attach either the actual form or the sources' standard or template copy.	

C.2. FDA Discretionary Waiver of consent The last two criteria above are almost impossible to meet in some circumstances. FDA provides waivers of consent only for emergencies or terrorism. FDA provided some leniency in enforcement (a discretionary waiver) of the consent requirements to studies meeting these tests. Does your activity qualify for their consent leniency?

1. Is an In Vitro Diagnostic device being studied? Is information to be submitted to FDA or held for their inspection being gathered?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
2. Is the investigational device exempt under 21 CFR 812.2(c)(3)? (It does not introduce energy into a subject and the result will not be used for diagnosis.)	<input type="checkbox"/> Yes <input type="checkbox"/> No	
3. Is this a waste or leftover specimen? From what is it a remnant? For what purpose was it originally taken? Has that purpose been fulfilled? If this project were not to occur, what would ordinarily happen to the specimen? (Waste or left-over implies something retrospective. Is the sample in the bank right now or will it be taken when your study gets under way?)	<input type="checkbox"/> Yes <input type="checkbox"/> No	The FDA "waiver" presumes consent for waste samples is impossible because the donors are long gone and unknown. It is IRC's understanding that FDA's guidance does NOT apply to prospective collection, that is, the samples will be obtained following IRB review.
4. When the first person on the research team receives the specimen, no donor can be individually identified. Correct? Are there any codes on the specimen or accompanying data? Does the supplier have written policies and procedures to prevent the release of identifying information?	<input type="checkbox"/> Yes <input type="checkbox"/> No	
5. Is the individual doing the study different from those caring for the patient? Could any information be shared?	<input type="checkbox"/> Yes <input type="checkbox"/> No	

If these 5 tests are met, a "pseudo-waiver" is possible. The IRB will need to consider if it can be waived in its entirety or if some tiny part of consent has been or can be obtained.

D. INFORMED CONSENT (NOTICE)

Informed consent can range from a signed 20-page document to a short verbal explanation followed by a yes nod before a venipuncture to a posted notice so that a person can refuse.

You may not know how – or even if – consent was obtained at the acquisition site. If you don't know, please answer to the best of your knowledge. If there was documented consent, a template or example is useful.

<p>1 At the time of original donation what kind of consent process or document could be expected? (e.g., a blood bank has donor cards and placards and advertising. University labs often have generic forms that include consent for future use.)</p>	
<p>2 If there was some sort of consent, might any of it have any consent element ranging from the word "research" to all the elements?</p>	
<p>3 Was there any offer of a chance to opt out of having the sample used for research? If yes, how was that tracked?</p>	
<p>4. Might there have been an implication that the sample would be used only for the original purpose?</p>	

Prospective sampling almost always requires consent.

Many methods other than a traditional consent form have been used to provide the information needed. A card or placard in a visible place, a line on a requisition form or a log initialed by the technician indicating that the information was given.

E SIGNATURES

I have made a good faith effort to learn the answers to these questions and to find out about the consent given at the time the specimen was taken. I have been honest, truthful and complete.

Signature & Date	
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F IRB REVIEWER (DO NOT USE)

Review Process:
 Expedited Review category 5: Materials collected solely for nonresearch purposes
 Expedited Review category _____
 Full board

<p>1 The study is approvable except for</p>	
<p>2. The consent process</p>	<p><input type="checkbox"/> was done under an IRB approval <input type="checkbox"/> can be "pseudo" waived: elements from FDA guidance are met <input type="checkbox"/> If neither checked, provide rationale and alternative:</p>
<p>3. Consent documentation</p>	<p><input type="checkbox"/> was done <input type="checkbox"/> with all elements or <input type="checkbox"/> partially <input type="checkbox"/> can be "pseudo" waived by FDA guidance <input type="checkbox"/> can be waived, 56.109(c)(1) the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context; <input type="checkbox"/> If no checks, provide rationale and alternative:</p>
<p>Signature & Date</p>	<p><input type="checkbox"/> Approve <input type="checkbox"/> Question – staff may judge response <input type="checkbox"/> Question – return to reviewer <input type="checkbox"/> Send to Full Board Comments:</p>