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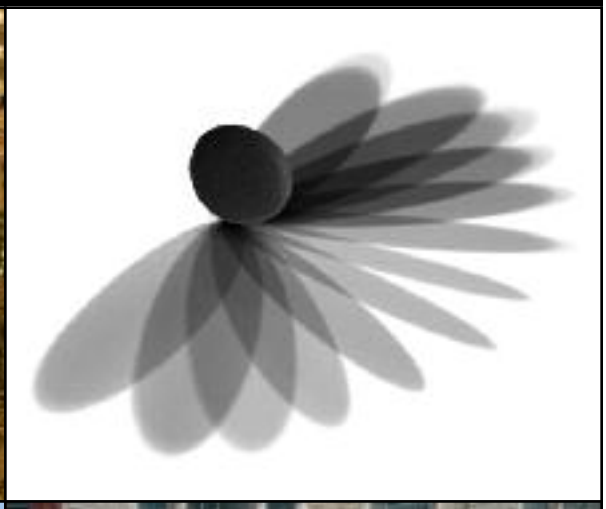
IRB Member and OPRS Staff Tip Sheets






University of Illinois at Chicago
Office for the Protection of Research Subjects

The tip sheets in this booklet provide a restatement of some frequently used regulations related to human subjects protection. Among other uses, OPRS staff use these tip sheets to answer regulatory questions and to conduct pre-reviews of protocols. IRB members use these tip sheets alongside expedited review guides and during convened IRB meetings in making their determinations. To enhance the transparency of the human subject protection program for investigators and potential subjects, the contents of this booklet are posted to the UIC OPRS website.

Andra M. Popa, JD, LLM, Assistant Director Quality Assurance/Quality Improvement
Margaret Moser, Assistant to the Vice Chancellor for Research
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Tip Sheet 1 • "111" IRB Approval Criteria

45 CFR 46.111(a) provides: "In order to approve research covered by this policy [the "Common Rule"] the IRB shall determine that all of the following requirements are satisfied:" (Please note that the industry interpretation of the term "approve" includes approval at both initial and continuing review).

Risks to subjects are minimized	1. "Risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes." (45 CFR 46.111(1)(i-ii)).
Risks to subjects are reasonable in relation to anticipated benefits	2. "Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of this responsibility." (45 CFR 46.111(a)(2)).
Selection of subjects is equitable	3. "Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons." (45 CFR 46.111(a)(3)).
Informed consent will be sought from each prospective subject	4. "Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by §46.116." (45 CFR 46.111(a)(4)). (Refer to Tip Sheet 5, Informed Consent Document Elements).
Informed consent will be appropriately documented	5. "Informed consent will be appropriately documented, in accordance with, and to the extent required by §46.117." (45 CFR 46.111(a)(5)).
As applicable:	
Additional safeguards are included for vulnerable populations	6. "When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled person, or economically or educationally disadvantaged persons, additional safeguards have been included in the study to protect the rights and welfare of these subjects." (45 CFR 46.111(b)).
Data Collection is monitored to ensure subject safety	7. "When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects." (45 CFR 46.111(6)). (Refer to Tip Sheet 2, Data & Safety Monitoring).

Tip Sheet 1 • "111" IRB Approval Criteria

45 CFR 46.111(a) provides: "In order to approve research covered by this policy [the "Common Rule"] the IRB shall determine that all of the following requirements are satisfied:" (Please note that the industry interpretation of the term "approve" includes approval at both initial and continuing review).

Privacy of subjects and confidentiality of data is protected	8. "When appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data." (45 CFR 46.111(7)).

Please note that the FDA [21 CFR 56.111(a)(b)(c)] and Veterans Administration [38 CFR 16.111(a)(b)(c)] have adopted the above. Yet, other additional requirements apply.

Tip Sheet 2 • Data & Safety Monitoring

When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

What is a Data and Safety Monitoring Plan?	
A Data and Safety Monitoring Plan (DSMP) is a general plan contained in the research protocol to ensure the safety of the subjects and to ensure the validity of the data. The essential elements of a data and safety monitoring plan are:	monitoring the progress of trial and the safety of participants;
	a description of the mechanism for reporting unanticipated problems involving risks to subjects or others (UPIRSOs), as well as adverse events, to the IRB, FDA, sponsor, and NIH, if applicable; and
	plans for assuring data accuracy and protocol compliance.
What is a Data Safety Monitoring Board or Data Monitoring Committee?	
The terms DSMB and DMC are synonymous and can be used interchangeably. A Data Safety Monitoring Board (DSMB) or Data Monitoring Committee (DMC) is a group of individuals with pertinent scientific expertise that:	reviews, on a regular basis, the accumulated research data from an ongoing clinical trial;
	advises the sponsor and/or researcher regarding the continuing safety of trial subjects and those yet to be recruited into the research trial; and
	advises as to the continuing validity and scientific merit of the trial.
Does every research protocol require a DSMP and a DSMB/DMC?	
Not all research protocols require a DSMP or a DSMB/DMC. Every investigator, however, should incorporate into the research protocol:	elements of a data and safety monitoring plan to ensure subject safety (i.e. safety monitoring and periodic assessments for safety);
	methods for reporting UPIRSOs; and
	measures to protect the confidentiality of the research data (i.e. privacy, coding, and storage).
	Also,
	As research protocols become more complicated and the level of risk to subjects increases, the investigator and the IRB have to evaluate the need for a DSMP and/or a DSMB/DMC. The regulations require that, in order to approve the research, the IRB must determine if the research plan makes adequate provisions for monitoring the data collected to ensure the safety of participants [45 CFR 46.11(s)(6), 21 CFR 56.111 (a)(6), 38 CFR 16 (a)(6)]. When appropriate, data and safety monitoring plans can be required for research in any discipline, including social and behavioral research.
	All research protocols conducted at the Clinical Research Center (CRC) are required to have a DSMP. For additional information regarding the requirements for conducting research at the CRC refer to the CRC web site or OPRS Appendix G.

Tip Sheet 2 • Data & Safety Monitoring

When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

When do the National Institutes of Health require DSMPs and DSMBs?

In general, the National Institutes of Health (NIH) believe that every clinical trial should have an IRB approved data and safety monitoring plan. The variety and type of monitoring plan may differ depending upon the nature, size, and complexity of the clinical trial being conducted.

A data and safety monitoring plan is required for all types of clinical trials, including physiologic, toxicity, and dose finding studies (Phase I); efficacy and safety studies (Phase II), and efficacy, effectiveness and comparative trials (Phase III).

The size and complexity of the monitoring committee or plan is also adjusted based upon the size or scope of the research. The monitoring may be conducted by the Principal Investigator or the NIH program staff for a small Phase I study, while a large Phase III clinical trial may require the establishment of an independent data and safety monitoring Board. However, even trials that pose little likelihood of harm should consider an external monitoring body.

The National Institutes of Health (NIH) requires the establishment of data safety monitoring boards for multi-site clinical trials involving interventions that entail potential risks to participants (generally Phase III clinical trials). For earlier phase trials (Phase I and Phase II), a DSMB may be appropriate if the studies involve multiple clinical sites, the studies are blinded or masked, or the studies involve high-risk interventions or vulnerable populations. A DSMB determines that the study is being conducted safely and effectively, and recommends early closure if significant risks have developed or if new information indicates that the trial is unlikely to be completed successfully.

Whatever the plan, IRBs should be provided feedback on a regular basis, usually at the time of continuing review. The feedback should include a summary of UPIRSOs, a summary of adverse events as required by NIH policy, and a copy of the DSMBs reports with any recommendations regarding the research. At a minimum, all monitoring plans must include a description of the reporting mechanisms for reporting adverse events to the IRB, the FDA, and the NIH. The investigator must ensure that the NIH is informed of any actions the IRB may take as a result of continuing review of the research.

Individual institutes within the NIH have their own policies regarding data and safety monitoring plans and data and safety monitoring boards, for example National Heart, Lung, and Blood Institute (NHLBI) revised their policy in May of 2005.

Tip Sheet 2 • Data & Safety Monitoring

When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

Does the Food and Drug Administration (FDA) require a DMC for clinical trials?	
	Current Food and Drug Administration (FDA) regulations do not require the use of data monitoring committees (DMC) in clinical trials except for research studies conducted in emergency settings in which the informed consent requirement is excepted [21 CFR 50.24(a)(7(iv)]. Research of this type is currently not allowed at UIC under UIC policy.
	The FDA believes that all clinical trials require safety monitoring (i.e. sponsor monitoring, medical monitors, adverse event reporting), but that not all trials require monitoring by a formal committee that is external to the trial organizers, sponsors, and investigators. DMCs are generally recommended for controlled clinical trials of any size that will compare rates of mortality or major morbidity, but a DMC is not required or recommended for most clinical trials. Additionally, DMCs are not generally needed for clinical trials that address lesser outcomes such as relief of symptoms, unless the clinical trial populations are at elevated risks of more severe outcomes.
	DMCs are not usually required in early Phase I and Phase II studies or pilot/feasibility studies, but formal monitoring groups may be appropriate for some early clinical studies, particularly if the risk level is higher than normal or the treatment approach is novel. These monitoring groups may be internal to the sponsor or consist of the investigators. Additionally, if the investigator is the manufacturer or the IND or IDE sponsor who presents the potential for financial or personal conflicts of interest, a DMC with independent members may provide added credibility to the oversight of subject safety and validity of the data.
Department of Defense	
	A research monitor is required for greater than minimal risk research, although the IRB can require for a portion of the project or for studies involving no more than minimal risk studies, if appropriate.
	An independent research monitor must be appointed by name.
	The research monitor has the authority to: (1) stop a research study in progress; (2) remove individuals from a study; and (3) take any steps to protect the safety and well being of subjects until the IRB can assess.

Tip Sheet 3 • Recruitment

Are recruitment procedures and materials fair and appropriate?

	Recruitment of subjects will be performed by research personnel with human subjects protection training and/or via contact initiated by subjects in response to recruitment materials and advertisements
	Recruitment methods, modes of communication, and materials are appropriate to the targeted subject population, including use of the population's primary language and/or reading level
	Adequate procedures are in place for minimizing coercion or undue influence, particularly when subjects are recruited via the investigator's own practice and/or medical, employment, or school records
	After initial recruitment contact, and as appropriate within the context of the research, subjects are given adequate opportunity to consider participating in the research before being asked to consent
	Recruitment materials and/or advertisements limit information to that necessary to determine eligibility and interest in the research (usually purpose of the research, summary of eligibility criteria and tasks/time commitment required of subjects, location of the research, and contact information for investigator/institution, a brief list of participation benefits)
	Recruitment materials and/or advertisements do NOT emphasize compensation either as direct payment, payment in kind (such as in "free" services or coupons for a product once it has been approved for marketing), "finder's fees" for referrals, and/or the payment of the amount to be paid by large or bold type
	Recruitment materials and/or advertisements do NOT imply that better treatment and/or an improved outcome will be a benefit of participation
	Recruitment materials and/or advertisements do NOT contain exculpatory language that waives, or appears to waive, any of the subject's legal rights or releases, or appears to release, the investigator, sponsor, or institution from liability for negligence
	For FDA-regulated research, recruitment materials are limited to claims consistent with FDA labeling and/or regarding the investigational nature of the research (for example: cannot state "new" treatment or drug)

Tip Sheet 4 • Reimbursement

Are compensation amounts and disbursement methods coercive or might they present undue influence?

	Compensation is NOT contingent upon the completion of the research
	Any "bonus" compensation is reasonable and NOT so large as to induce subjects to stay in the research when the subjects would have otherwise withdrawn
	All information regarding compensation, including a schedule of the amount and timing of payments, is accurately detailed in the consent document(s)
	Compensation for referrals ("finder's fees"), both in amount and in disbursement method, is reasonable and appropriate within the context of the research. Any payments to professionals in exchange for referrals of prospective payments ("finders fees") are prohibited, unless they are judged not to increase the possibility of coercion of undue influence on subjects by using unreasonable compensation or unreasonable conditions for distribution of compensation.
	Compensation that is related to the timing or rate of enrollment ("bonus payments"), both in amount and in disbursement method, is reasonable and appropriate within the context of the research
	Compensation via "lottery" or by random drawing is discouraged unless the amount, the odds of being compensated, the method of disbursement, and any increase in risk (such as from a breach of privacy and/or confidentiality due to the retention of subject contact information) are clearly stated in the consent document(s), AND the amount and method are reasonable and appropriate within the context of the research AND it is not likely to induce subjects to participate in the research if they would have otherwise declined
	Compensation is prohibited when research is integrated into subject's standard care and does not make special demands on the subject beyond those of usual care
	Compensation from sponsors to the investigator and/or UIC that are based on the timing or rate of subject enrollment are prohibited unless they do NOT increase the possibility of coercion or undue influence of the investigators OR the subjects
	If Department of Defense sponsored research includes US military personnel note: (1) limitations on dual compensation for US military personnel prohibits an individual from receiving pay from mor than one position for more than 40 hours of work in one calendar week; and (2) this limitation includes temporary, part-time, and intermittent appointments.

Tip Sheet 5 • Informed Consent Document Elements

8 Basic Elements of Informed Consent (45 CFR 46.116(a)(1)-(8), prohibition against exculpatory language, and signature line:	
	1a. A statement that the study involves research
	1b. An explanation of the purposes of the research
	1c. The expected duration of the subject's participation
	1d. A description of the procedures to be followed
	1e. Identification of any procedures which are experimental (if relevant)
	2. A description of any reasonably foreseeable risks or discomforts to the subject
	3. A description of any benefits to the subject or to others which may reasonably be expected from the research
	4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject
	5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained
	6. For research involving more than minimal risk, an explanation as to whether any compensation, and an explanation as to whether any medical treatments are available, if injury occurs and, if so, what they consist of, or where further information may be
	7a. States who to contact for questions, concerns, or complaints about the research
	7b. States who to contact for questions about subject's rights (usually OPRS)
	7c. States who to contact in the event of a research-related injury to the subject (if relevant)
	8a. States that participation is voluntary
	8b. States that there are no penalties or loss of benefits for refusal to participate in some or all of the research procedures and/or for discontinuing participation of some or all of the research procedures
	No exculpatory language can be included in the consent form
	A signature is required - the consent document must include the appropriate signature lines

Additional elements, as appropriate (45 CFR 46.116(b)):	
	A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant), which are currently unforeseeable
	Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent
	Any additional costs to the subject that may result from participation in the research
	The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject
	A statement that significant new findings developed during the course of the research, which may relate to the subject's willingness to continue participation, will be provided to the subject
	Amount and schedule of subject payments
	Template UIC language concerning subject injury
	The approximate number of subjects involved in the study at UIC, as well as study-wide

Tip Sheet 5 • Informed Consent Document Elements

UIC Required Elements (some only if applicable)	
	Reading level and/or visual content appropriate to the prospective subject population
	A footer on every page of the consent with a brief title, version #, date, protocol #, if available, and page number in an x of y format.
	If the research is funded, states the name of the sponsor or funding agency
	Statement of how the prospective subject was identified/ why being asked
	Template statement for focus group, when applicable
	Template statement for UIC students, when applicable
	Template statement for UIC employees, when applicable
	If applicable, statement as to reproductive risks and precautions required
	If applicable, warning statement for individuals who will be taking the drug home
	Discloses conflicts of interest, if any (as per the SEAM, if applicable, and with IRB approval)
	If applicable, discloses genetic testing and the subject has a separate "check off" as to genetic testing. Discloses whether the subject will be given the results. States whether the results may make the subjects upset. Instructs whether counseling will be provided.
	If applicable, discloses banking of tissue [includes blood, body fluids, DNA] and the subject has a separate "check off" section as to tissue banking, future use, identifiers, and whether they can be contacted for future studies
	If applicable, statement as to fluctuating capacity
	If a Certificate of Confidentiality/Privacy Certificate has been obtained, states the terms and limitations provided by the Certificate

Tip Sheet 5 • Informed Consent Document Elements

On Separate VA Consent Template **If JBVAMC research, additional required elements of informed consent (VA regulations):**	
	Uses the VA template [10-1086] for informed consent
	Includes VA-required language regarding injury, compensation, confidentiality, and cost:
	a. VA-approved subject injury language
	b. Some veterans pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to standard medical care and services provided by the VA that are not part of this study. You will be expected to pay these costs according to your usual method of payment. Except for required co-payments, there are no additional costs to you for being part of this study.
	c. Includes the following language: If you participate in the research, your authorization will be required to have access to your private medical records. You will be asked to sign a separate authorization form to allow us to have this access. If you do not provide this authorization, you may not participate in the research.
	Includes contact information for VA patient advocate, R&D committee, and UIC OPRS
If FDA-regulated research, additional elements of informed consent (FDA regulations and UIC requirements):	
	States that FDA, industry sponsor, and/or other appropriate agencies (for example, NIH, CDC) may inspect research records for verification and accuracy of information
	Identifies experimental agents and/or procedures (FDA regulation). If the research involves an investigational drug, device, biologic, or HUD, states the regulatory status of the agent using explanations designed to be understood by the targeted subject population, including lay definitions of terms of art (UIC required element)
	If applicable, states whether biological materials will be used for commercial purposes
If applicable, insert Genome-Wide Association Studies (GWAS) language, address GWAS points.	

Tip Sheet 6 • Informed Consent Waiver or Alteration

Do informed consent procedures and materials justify granting an alteration or waiver of informed consent?

Either All Elements of Option 1 or the Element of Option 2 must be true to grant an alteration or waiver of informed consent:	
Option 1	An alteration (for example, use of consent materials that do not contain all of the elements of consent) or waiver of informed consent would not adversely affect the rights or welfare of subjects
	If an alteration or waiver is not granted, it would be so difficult as to be nearly impossible to conduct the research and/or the research would present additional risk to subjects (for example, increased risk of a breach of confidentiality)
	If appropriate, subjects will be provided with relevant information about the research after participation
Option 2	Research is conducted under the direction of state or local government officials and is designed to study public benefit/service programs, procedures for obtaining public benefits/services, changes or alternatives to public
As applicable:	
FDA Regulated	For FDA-regulated research, alterations or waivers are NOT permitted unless the research falls within an exception, the research qualifies for emergency use of a test article, OR research qualifies for in vitro diagnostic device with specimens that are not individually identifiable
Deception in Research	Criteria for alteration of consent must be satisfied, among other criteria
Research Sponsored by the Department of Defense	If the research subject meets the definition of "experimental subject," a waiver of consent is prohibited unless a waiver is obtained from the Secretary of Defense. If the research subject does not meet the definition of "experimental subject," the IRB may waive consent.

Tip Sheet 7 • Waiver of Documentation of Informed Consent

An IRB may waive the requirement to document informed consent if it finds that one of these criteria is met:

OHRP 45 CFR 46.117(c)(1)	For research not subject to FDA regulation, the IRB finds:
	That the only record linking the subjects and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern.
OHRP 45 CFR 46.117(c)(2)	**For research subject to FDA 21 CFR 56.109(c)(1), the IRB finds:**
	For research subject either to OHRP or FDA regulation, the IRB finds: That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.
Research Sponsored by the Department of Defense	If the research subject meets the definition of "experimental subject," a waiver of consent is prohibited unless a waiver is obtained from the Secretary of Defense. If the research subject does not meet the definition of "experimental subject," the IRB may waive consent.

Tip Sheet 8 • Informed Consent Process

Are informed consent procedures and materials fair and appropriate?	
	The application form identifies who will obtain informed consent and verifies that consent is obtained by research personnel with human subjects protection training
	Language and/or reading level
	Adequate procedures are in place for minimizing coercion or undue influence
	Consent does NOT include exculpatory language and/or appear to release the investigator, sponsor, institution and/or its agents from any legal liability (45 CFR 116)
OHRP's Examples of Inappropriate Language	
	By agreeing to this use, you should understand that you will give up all claim to personal benefit from commercial or other use of these substances.
	I voluntarily and freely donate any and all blood, urine, and tissue samples to the U.S. Government and hereby relinquish all right, title, and interest to said items.
	By consent to participate in this research, I give up any property rights I may have in bodily fluids or tissue samples obtained in the course of the research.
	I waive any possibility of compensation for injuries that I may receive as a result of participation in this research.
OHRP's Examples of Appropriate Language	
	Tissue obtained from you in this research may be used to establish a cell line that could be patented and licensed. There are no plans to provide financial compensation to you should this occur.
	By consenting to participate, you authorize the use of your bodily fluids and tissue samples for the research described above.
	This hospital is not able to offer financial compensation nor to absorb the costs of medical treatment should you be injured as a result of participating in this research.
	This hospital makes no commitment to provide free medical care or payment for any unfavorable outcomes resulting from participation in this research. Medical services will be offered at the usual charge.

Tip Sheet 9 • 21 CFR 50.23

FDA Exception from general consent requirements

(a) The obtaining of informed consent shall be deemed feasible unless, before use of the test article (except as provided in paragraph (b) of this section), both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following:

	(1) The human subject is confronted by a life-threatening situation necessitating the use of the test article.
	(2) Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject.
	(3) Time is not sufficient to obtain consent from the subject's legal representative.
	(4) There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject.

(b) If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (a) of this section in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation.

(c) The documentation required in paragraph (a) or (b) of this section shall be submitted to the IRB within 5 working days after the use of the test article.

(d)(1) Under 10 U.S.C. 1107(f) the President may waive the prior consent requirement for the administration of an investigational new drug to a member of the armed forces in connection with the member's participation in a particular military operation. The statute specifies that only the President may waive informed consent in this connection and the President may grant such a waiver only if the President determines in writing that obtaining consent: Is not feasible; is contrary to the best interests of the military member; or is not in the interests of national security. The statute further provides that in making a determination to waive prior informed consent on the ground that it is not feasible or the ground that it is contrary to the best interests of the military members involved, the President shall apply the standards and criteria that are set forth in the relevant FDA regulations for a waiver of the prior informed consent requirements of section 505(i)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)(4)).

Tip Sheet 9 • 21 CFR 50.23

FDA Exception from general consent requirements

Before such a determination may be made that obtaining informed consent from military personnel prior to the use of an investigational drug (including an antibiotic or biological product) in a specific protocol under an investigational new drug application (IND) sponsored by the Department of Defense (DOD) and limited to specific military personnel involved in a particular military operation is not feasible or is contrary to the best interests of the military members involved the Secretary of Defense must first request such a determination from the President, and certify and document to the President that the following standards and criteria contained in paragraphs (d)(1) through (d)(4) of this section have been met.

	(i) The extent and strength of evidence of the safety and effectiveness of the investigational new drug in relation to the medical risk that could be encountered during the military operation supports the drug's administration under an IND.
	(ii) The military operation presents a substantial risk that military personnel may be subject to a chemical, biological, nuclear, or other exposure likely to produce death or serious or life-threatening injury or illness.

(iii) There is no available satisfactory alternative therapeutic or preventive treatment in relation to the intended use of the investigational new drug."

	(iv) Conditioning use of the investigational new drug on the voluntary participation of each member could significantly risk the safety and health of any individual member who would decline its use, the safety of other military personnel, and the accomplishment of the military mission.
	(v) A duly constituted institutional review board (IRB) established and operated in accordance with the requirements of paragraphs (d)(2) and (d)(3) of this section, responsible for review of the study, has reviewed and approved the investigational new drug protocol and the administration of the investigational new drug without informed consent. DOD's request is to include the documentation required by 56.115(a)(2) of this chapter.

Tip Sheet 10 • 21 CFR 50.24

FDA Exception from Informed Consent Requirements for Emergency Research

(a) The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:"	
(1) The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.	
(2) Obtaining informed consent is not feasible because:	
	(i) The subjects will not be able to give their informed consent as a result of their medical condition;
	(ii) The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
	(iii) There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.
(3) Participation in the research holds out the prospect of direct benefit to the subjects because:	
	(i) Subjects are facing a life-threatening situation that necessitates intervention;
	(ii) Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
	(iii) Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity.
(4) The clinical investigation could not practicably be carried out without the waiver.	

FDA Exception from Informed Consent Requirements for Emergency Research

(5) The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review.

(6) The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with 50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (a)(7)(v) of this section.

(7) Additional protections of the rights and welfare of the subjects will be provided, including, at least:

	(i) Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn;

(ii) Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits;

FDA Exception from Informed Consent Requirements for Emergency Research

(iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;	
	(iv) Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and
	(v) (a) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.
	(b) The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible.

FDA Exception from Informed Consent Requirements for Emergency Research

(iii) Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results;	
	If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.
	(c) The IRB determinations required by paragraph (a) of this section and the documentation required by paragraph (e) of this section are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with 56.115(b) of this chapter.
	(d) Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under 312.30 or 812.35 of this chapter.
	(e) If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, and to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

Tip Sheet 11 • Research Involving Children

Table: Approval Criteria for Categories of Research Involving Children

Category 1: Research Not Involving Greater than Minimal Risk (45 CFR 46.404; 21 CFR 50.51)	
Permission of one parent is permitted if approved by the IRB	1. The research presents no more than minimal risk to the children; and 2. Adequate provisions are made for soliciting the assent of the children and permission of their parents or legal guardians as set forth at 46.408.
Category 2: Research Involving Greater than Minimal Risk but Presenting the Prospect of Direct Benefit to the Individual Child (45 CFR 46.405; 21 CFR 50.52)	
Permission of one parent is permitted if approved by the IRB.	1. The research presents more than minimal risk to the children by an intervention or procedure that holds out the prospect of direct benefit for the individual child, or by a monitoring procedure that is likely to contribute to the child's well-being; 2. The risk is justified by the anticipated benefit to the child; 3. The relation of the anticipated benefit to the risk is at least as favorable to the children as that presented by available alternative approaches; and 4. Adequate provisions are made for obtaining the assent of the child and permission of their parents or legal guardians as set forth at 46.408
Category 3: Research Involving Greater than Minimal Risk and No Prospect of Direct Benefit to the Individual Child, but Likely to Yield Generalizable Knowledge about the Child's Disorder or Condition. (45 CFR 46.406; 21 CFR 50.53)	
Permission of both parents is required unless: 1. One parent is deceased, unknown, incompetent, not reasonably available, or 2. Only one parent has legal responsibility for care and custody of child.	1. Greater than minimal risk is presented by an intervention or procedure that does not hold out the prospect of direct benefit for the individual child, or by a monitoring procedure which is not likely to contribute to the well-being of the child; 2. Risk represents a minor increase over minimal risk; 3. Intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations; 4. Intervention or procedure is likely to yield generalizable knowledge about the subjects' disorder or condition which is of vital importance for the understanding or amelioration of the subjects' disorder or condition; and 5. Adequate provisions are made for soliciting assent of the children and permission of their parents or legal guardians.

Table: Approval Criteria for Categories of Research Involving Children

Category 4: Research Not Otherwise Approvable, which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem Affecting the Health or Welfare of Children (45 CFR 46.407 and 21 CFR 50.54)	
Permission of both parents is required unless: 1. One parent is deceased, unknown, incompetent, not reasonably available, or 2. Only one parent has legal responsibility for care and custody of the child. For research that is not federally funded or under the purview of the FDA, and the IRB determines such research falls within category 46.407, the UIC IRB will provide copies of the protocol and the IRB minutes to the HPA for a determination regarding whether an ad hoc panel of experts should be convened to review the research in a process parallel to that of OHRP expert panel review. In this case, UIC IRB approval will not be released until either the HPA determines an ad hoc panel is not necessary or the ad hoc panel issues a recommendation that the research is acceptable.	For research where the IRB finds the research does not meet the requirements set forth in categories 46.404, 46.405 or 46.406 as described above in this table, the IRB may approve the research only if: 1. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; and 2. If Federally funded or under the purview of the FDA, the Secretary of DHHS or, if applicable, FDA Commissioner, after consultation with a panel of experts in pertinent disciplines and following opportunity for public review and comment, has determined either: A. That the research in fact satisfies the conditions of categories 46.404, 46.405, or 46.406; or B. The following: 1. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children; 2. The research will be conducted in accordance with sound ethical principles; and 3. Adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.
For VA Research Only: If the study involves children, a CRADO waiver is required and the research can involve only minimal risk research.	

Tip Sheet 12 • Research Involving Pregnant Women, Fetuses, and Neonates

Definitions	Neonate means a newborn, (45 CFR 46.202) Viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration.
Neonates of Uncertain Viability and Nonviable Neonates may be involved in research if all of the following conditions are met:	1.Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates.
	2.Each individual providing consent under paragraph (b)(2) or (c)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate.
	3.Individuals engaged in the research will have no part in determining the viability of a neonate.
	4.The requirements of paragraph (b) or (c) of this section have been met as applicable. (See below)
Neonates of Uncertain Viability: Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions have been met:	1.The IRB determines that: i. The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, OR ii. The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research AND
	2.The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest.
Nonviable Neonates: After delivery a nonviable neonate may not be involved in research covered by this subpart unless ALL of the following additional conditions are met:	1. Vital functions of the neonate will not be artificially maintained;
	2. The research will not terminate the heartbeat or respiration of the neonate;
	3. There will be no added risk to the neonate resulting from the research;
	4. The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; AND
	5. The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of Sec. 46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5).

Tip Sheet 12 • Research Involving Pregnant Women, Fetuses, and Neonates

Viable Neonates:	A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of the Federal Policy for Protection of Human Subjects (Subpart A) and Protections for Children Involved as Subjects (Subpart D). (That is, viable neonates may be considered for participation in research according to the same regulations applied other minors.)
Pregnant Women or Fetuses may be involved in research if all of the following conditions are met:	(a) Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;
	(b) The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means;
	(c) Any risk is the least possible for achieving the objectives of the research;
	(d) If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart A of this part;
	(e) If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.
	(f) Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate;
	(g) For children as defined in Sec 46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part;
	(h) No inducements, monetary or otherwise, will be offered to terminate a pregnancy;
	(i) Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
	(j) Individuals engaged in the research will have no part in determining the viability of a neonate

Tip Sheet 13
OHRP Guidance on the Involvement of Prisoners in Research (Reprinted) • May 23, 2003

Scope: This document describes the requirements of Department of Health and Human Services (HHS) regulations at 45 CFR part 46, subpart C, which provides additional protections to prisoners involved as subjects in HHS-conducted or supported research. For further information: OHRP Prisoner Research Contact Person at (301) 496-7005 (phone); (301) 402-0527(fax)

General Regulatory Background	HHS regulations at 45 CFR part 46, subpart C provide additional protections pertaining to biomedical and behavioral research involving prisoners as subjects. The regulations are applicable to all biomedical and behavioral research conducted or supported by HHS. See 45 CFR 46.301. It is important to note that the regulations provide that "biomedical or behavioral research conducted or supported by HHS shall not involve prisoners as subjects" unless the research is specifically authorized within the subpart. See 45 CFR 46.306(b). In the preamble to the final subpart C rule, the drafters noted: "In fact, most testimony before the Commission opposed the use of prisoners in any form of medical research not intended to benefit the individual prisoner," (November 16, 1978). HHS did determine that some limited research would be permissible but not "until additional and more stringent review procedures are conducted."
Subpart C applies where any subject is or becomes a prisoner	The provisions of subpart C apply to any research conducted or supported by HHS in which prisoners are subjects. This includes situations where a human subject becomes a prisoner after the research has commenced. As the Purpose section of the regulation notes: "Inasmuch as prisoners may be under constraints because of their incarceration which could affect their ability to make a truly voluntary and uncoerced decision whether or not to participate as subjects in research, it is the purpose of this subpart to provide additional safeguards for the protection of prisoners involved in activities to which this subpart is applicable." 45 CFR 46.302. These concerns apply whether the research involves individuals who are prisoners at the time of enrollment in the research or who become prisoners after they become enrolled in the research. In the latter situation, it is unlikely that review of the research and the consent document contemplated the constraints imposed by incarceration.
What does the definition of prisoner encompass?	"Prisoner" is defined by HHS regulations at 45 CFR part 46.303(c) as "any individual involuntarily confined or detained in a penal institution. The term is intended to encompass individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing."
Special Composition of IRB	At least one member of the IRB must be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one IRB, only one IRB need satisfy this requirement. In the absence of choosing someone who is a prisoner or has been a prisoner, the IRB should choose a prisoner representative who has a close working knowledge, understanding and appreciation of prison conditions from the perspective of the prisoner. For research involving prisoners as subjects, the IRB must meet the special composition requirements of 45 CFR 46.304 for all types of review of the protocol, including initial review, continuing review, review of protocol amendments, and review of reports of unanticipated problems involving risks to subjects.

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Additional duties of the IRB where prisoners are involved. When an IRB is reviewing a protocol in which a prisoner is a subject, the IRB must make, in addition to other requirements under 45 CFR 46, subpart A, seven additional findings under 45 CFR 46.305(a), as follows:	(1) the research under review represents one of the categories of research permissible under 45 CFR 46.306(a)(2);
	(2) any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;
	(3) the risks involved in the research are commensurate with risks that would be accepted by nonprisoner volunteers;
	(4) procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the IRB justification in writing for following some other procedures, control subjects must be selected randomly from the group of available prisoners who meet the characteristics needed for that particular research project;
	(5) the information is presented in language which is understandable to the subject population;
	(6) adequate assurance exists that parole boards will not take into account a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and
	(7) where the IRB finds there may be a need for follow-up examination or care of participants after the end of their participation, adequate provision has been made for such examination or care, taking into account the varying lengths of individual prisoners' sentences, and for informing participants of this fact.
Permitted research involving prisoners.	For research conducted or supported by HHS to involve prisoners, two actions must occur: (1) the institution engaged in the research must certify to the Secretary (through OHRP) that the IRB designated under its assurance of compliance has reviewed and approved the research under 45 CFR 46.305; and (2) the Secretary (through OHRP) must determine that the proposed research falls within the categories of research permissible under 45 CFR 46.306(a)(2).

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The categories of permissible research	(i) study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects; "Minimal risk" is the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.
	(ii) study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
	(iii) research on conditions particularly affecting prisoners as a class (for example, vaccine trials and other research on hepatitis which is much more prevalent in prisons than elsewhere; and research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults) provided that the study may proceed only after the Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research; or (iv) research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject. In cases in which those studies require the assignment of prisoners in a manner consistent with protocols approved by the IRB to control groups which may not benefit from the research, the study may proceed only after the Secretary (through OHRP) has consulted with appropriate experts including experts in penology, medicine, and ethics, and published notice, in the Federal Register, of his intent to approve such research.
Documentation of IRB Findings.	Pursuant to HHS regulations at 45 CFR 46.115(a), an institution or, when appropriate, an IRB, shall prepare and maintain adequate documentation of IRB activities. For the purposes of subpart C, the IRB activities include making the specific findings required under HHS regulations at 45 CFR 46.305(a). OHRP would consider documentation of protocol-specific information justifying each IRB finding required under 45 CFR 46.305(a) to be one way of adequately documenting the IRB activities required under subpart C.

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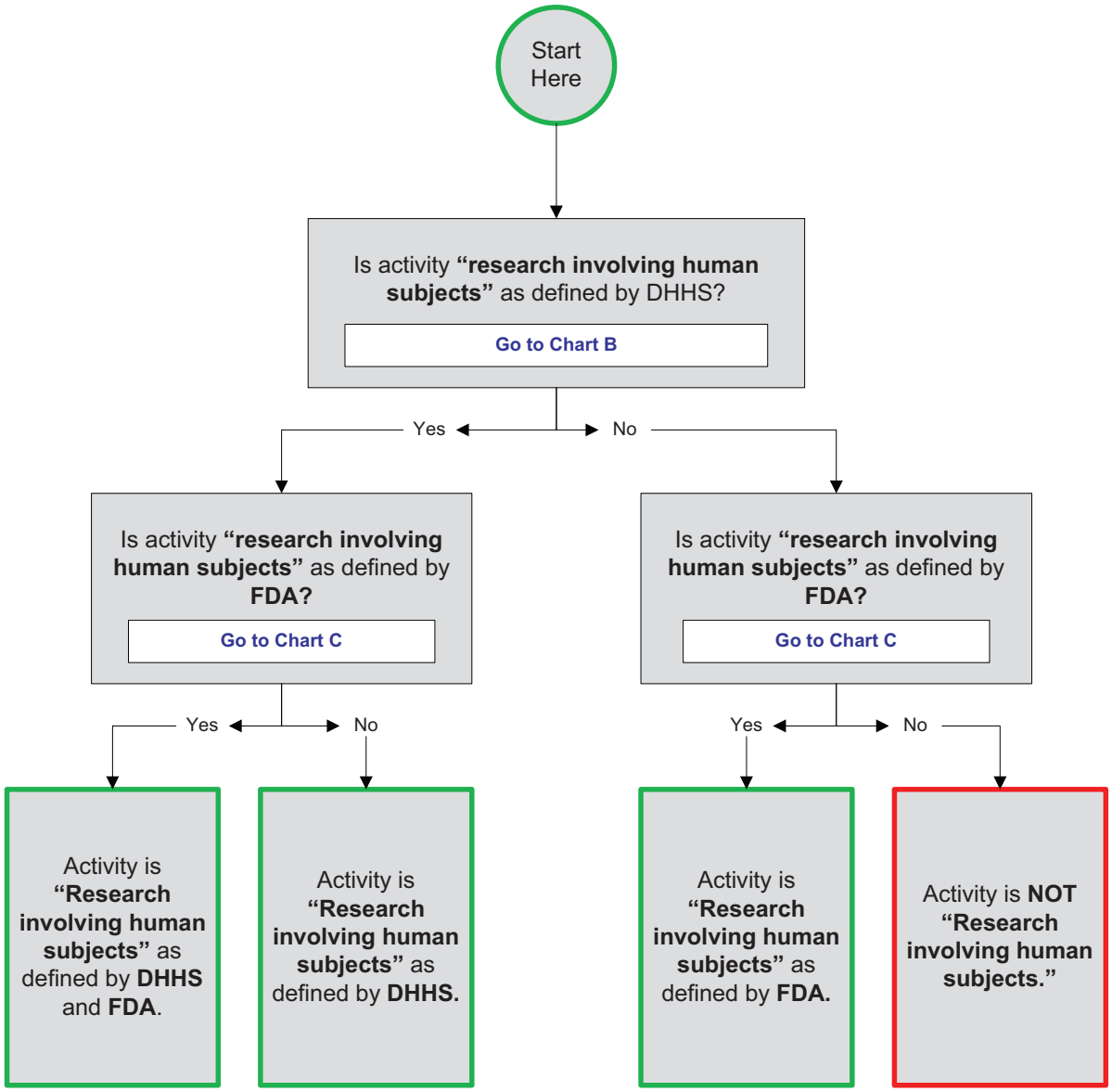
Responsibilities of Institutions.	Maintain a record of the determination of the IRB regarding the seven additional findings required under HHS regulations at 45 CFR 46.305(a). Under 45 CFR 46.305(c), the institution responsible for conducting research involving prisoners that is supported by HHS shall certify to the Secretary (through OHRP) that the IRB has made the seven findings required under 45 CFR 46.305(a). The institution must send to OHRP a certification letter to this effect, which should also include the name and address of the institution and specifically identify the research protocol in question and any relevant HHS grant application or protocol. HHS conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its approval in writing to the institution on behalf of the Secretary under 45 CFR 46.306(a)(2). Under its authority at 45 CFR 46.115(b), OHRP requires that the institution responsible for the conduct of the proposed research also submit to OHRP a copy of the research proposal so that OHRP can determine whether the proposed research involves one of the categories of research permissible under 45 CFR 46.306(a)(2), and if so, which one. The term "research proposal" includes the IRB-approved protocol, any relevant HHS grant application or proposal, any IRB application forms required by the IRB, and any other information requested or required by the IRB to be considered during initial IRB review.
Responsibilities of OHRP.	Following receipt of the research proposal, OHRP will determine which, if any, of the four categories of research permissible under HHS regulations at 45 CFR 306(a)(2) the proposed research meets. OHRP will consult with appropriate experts with respect to certain research that falls under paragraphs (iii) and (iv) of 45 CFR 46.306(a)(2).

Tip Sheet 14 • Decision Tree: Are You Conducting Human Subjects Research as Defined by DHHS or FDA?

Is human subjects research being conducted as defined by HHS or the FDA?

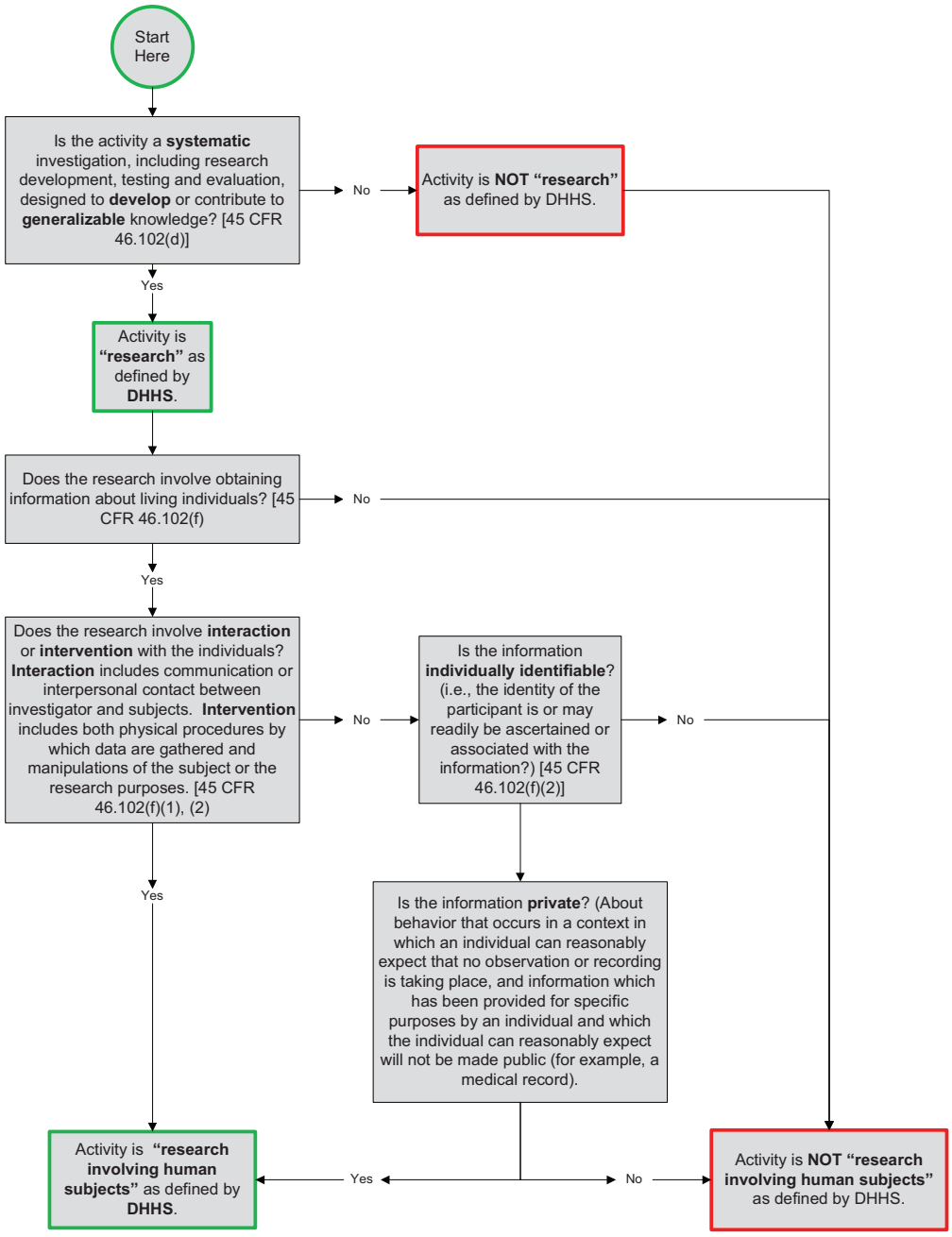
Chart A



Tip Sheet 14 • Decision Tree:
Are You Conducting Human Subjects Research as Defined by DHHS or FDA?

Is human subjects research being conducted as defined by HHS or the FDA?

Chart B



Tip Sheet 14 • Decision Tree:
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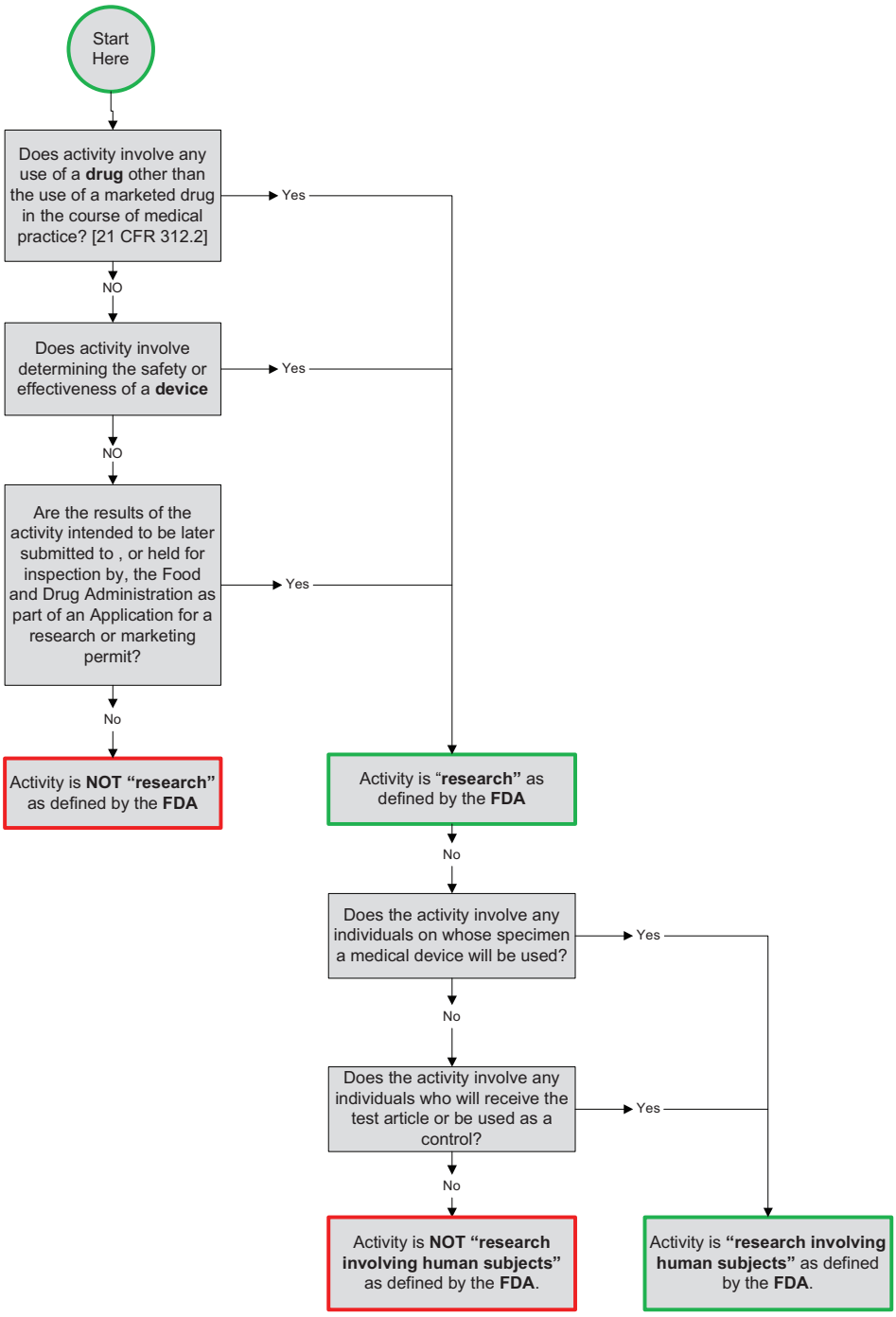
Is human subjects research being conducted as defined by HHS or the FDA?

Chart C



Tip Sheet 15 • Exempt Categories

Select the exempt category for research eligible for exempt review.

(b) Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:

(1) Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

(2) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, unless:

	(i) information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; **AND**
	(ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

(3) Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, if:

	(i) the human subjects are elected or appointed public officials or candidates for public office; or
	(ii) federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

(4) Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects. For VA Research, if exemption category 4 is claimed, the investigator may not retain any of the 18 identifiers outlined in the HIPAA Privacy Rule, and the investigator may not have access to any code by which the information may be linked to individuals. When the investigator will review PHI for the research, a waiver of authorization is required.

Tip Sheet 15 • Exempt Categories

Select the exempt category for research eligible for exempt review.

(5) Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:	
	(i) Public benefit or service programs;
	(ii) procedures for obtaining benefits or services under those programs;
	(iii) possible changes in or alternatives to those programs or procedures; or
	(iv) possible changes in methods or levels of payment for benefits or services under those programs.
(6) Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.	
(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.	
The following categories apply only to research being reviewed at continuing review	
(8)(a) ALL of the following are true: the research is permanently closed to the enrollment of new subjects; all subjects have completed all research-related interventions; and the research remains active only for long-term follow-up of subjects.	
(8)(b) No subjects have been enrolled and no additional risks have been identified.	
(8)(c) The remaining research activities are limited to data analysis.	
(9) All of the following are true: the research is not conducted under an investigational new drug application or investigational device exemption; the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified; and is this research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product?	

Tip Sheet 16 • Expedited Categories

Select the expedited category for research eligible for expedited review.

<table>
<tr><td colspan="2">I. The seven expedited initial review categories are:</td></tr>
<tr><td colspan="2">(1) Clinical studies of drugs and medical devices only when condition (a) or (b) is met.</td></tr>
<tr><td rowspan="2"></td><td>(a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (Note: Research on marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review.)</td></tr>
<tr><td>(b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.</td></tr>
<tr><td colspan="2">(2) Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture as follows:</td></tr>
<tr><td rowspan="2">Category 2 study must not involve children in surveys OR the researcher must not participate or manipulate the study</td><td>(a) from healthy, nonpregnant adults who weigh at least 110 pounds. For these subjects, the amounts drawn may not exceed 550 ml in an 8 week period and collection may not occur more frequently than 2 times per week; or</td></tr>
<tr><td>(b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml per kg in an 8 week period and collection may not occur more frequently than 2 times per week.</td></tr>
<tr><td colspan="2">(3) Prospective collection of biological specimens for research purposes by noninvasive means.</td></tr>
<tr><td></td><td>Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.</td></tr>
</table>

Tip Sheet 16 • Expedited Categories

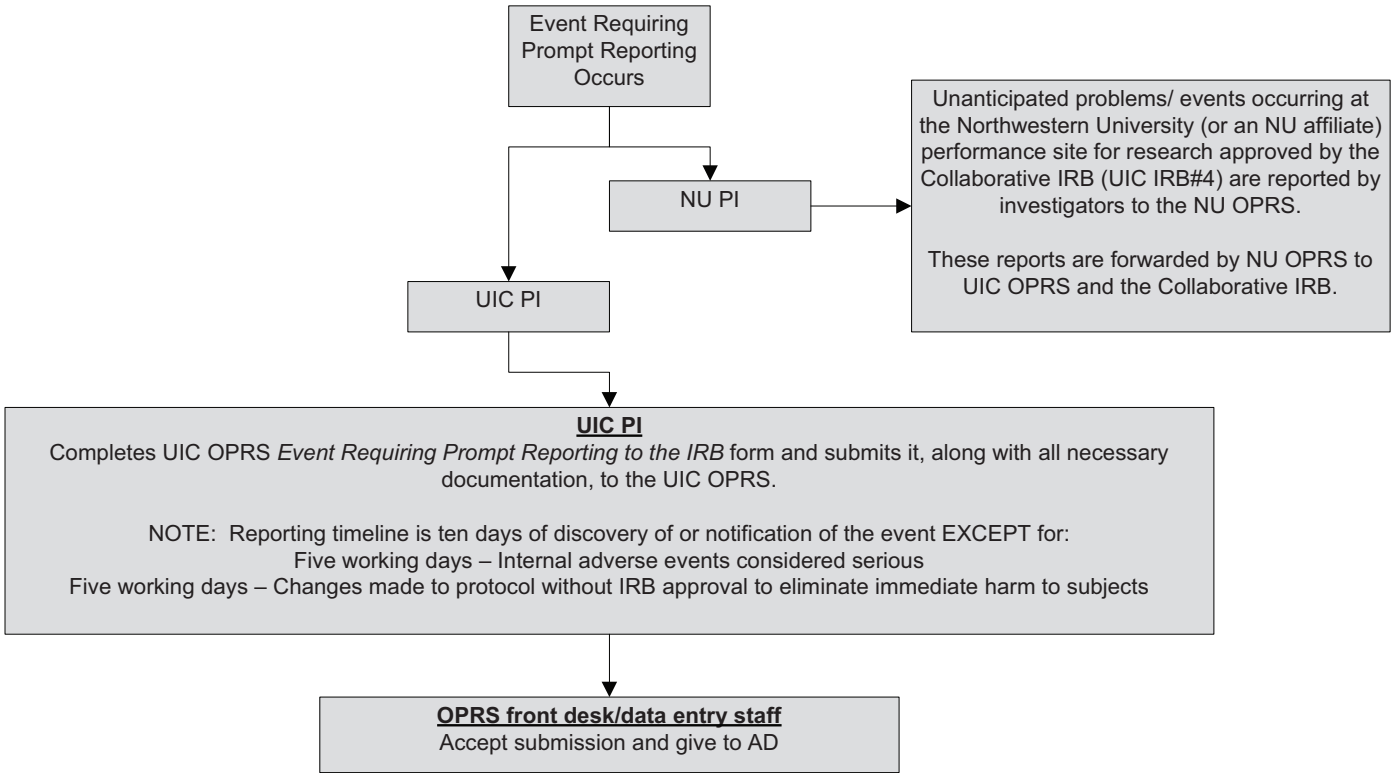
Select the expedited category for research eligible for expedited review.

(4) Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)	
	Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.
(5) Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis). (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(4). This listing refers only to research that is not exempt.)	
(6) Collection of data from voice, video, digital, or image recordings made for research purposes.	
(7) Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies. (NOTE: Some research in this category may be exempt from the HHS regulations for the protection of human subjects. 45 CFR 46.101(b)(2) and (b)(3). This listing refers only to research that is not exempt.)	

Tip Sheet 17 • Prompt Reporting Process and Definition of Terms

What is the appropriate procedure for Prompt Reporting?

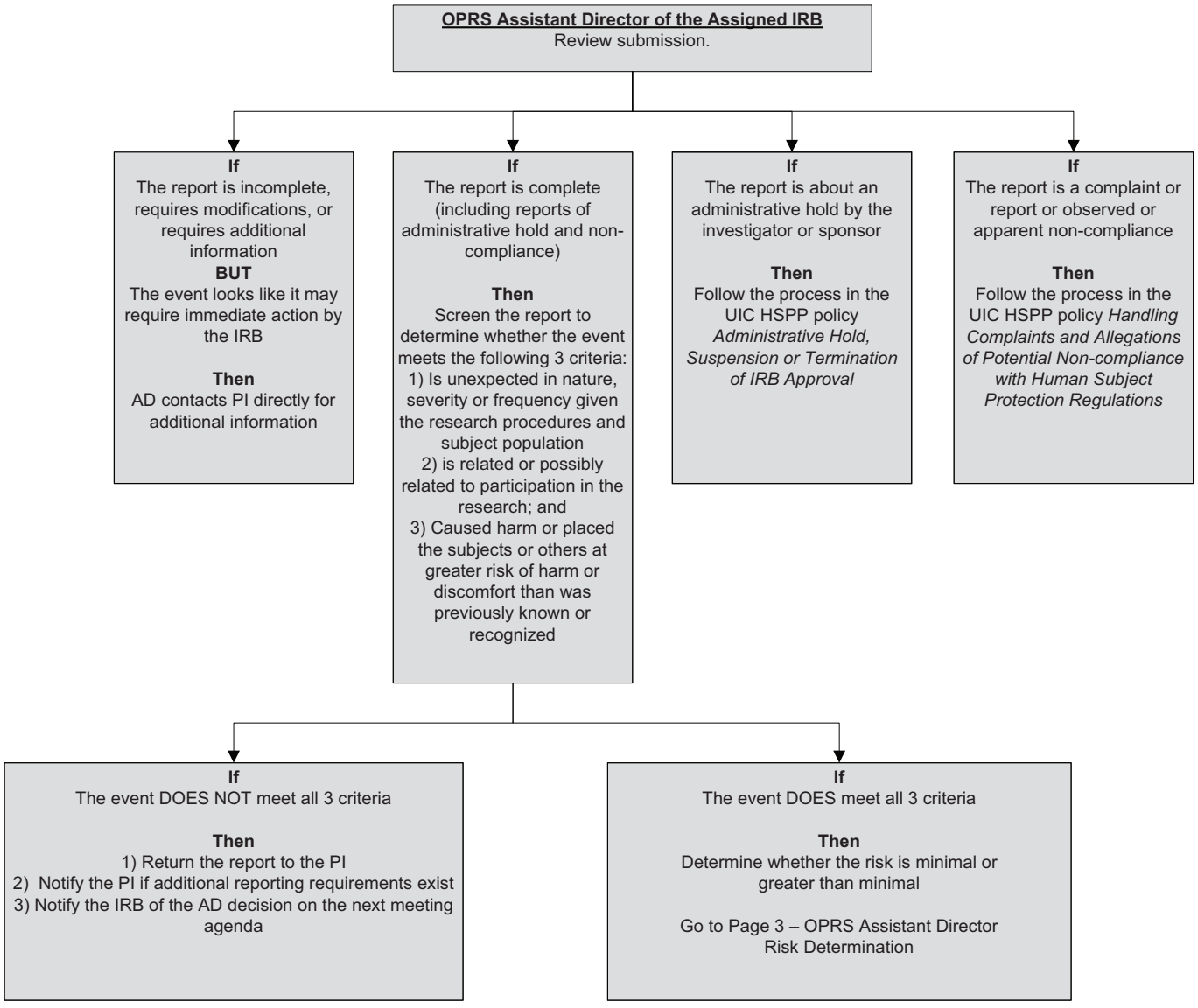
Chart A



Tip Sheet 17 • Prompt Reporting Process and Definition of Terms

What is the appropriate procedure for Prompt Reporting?

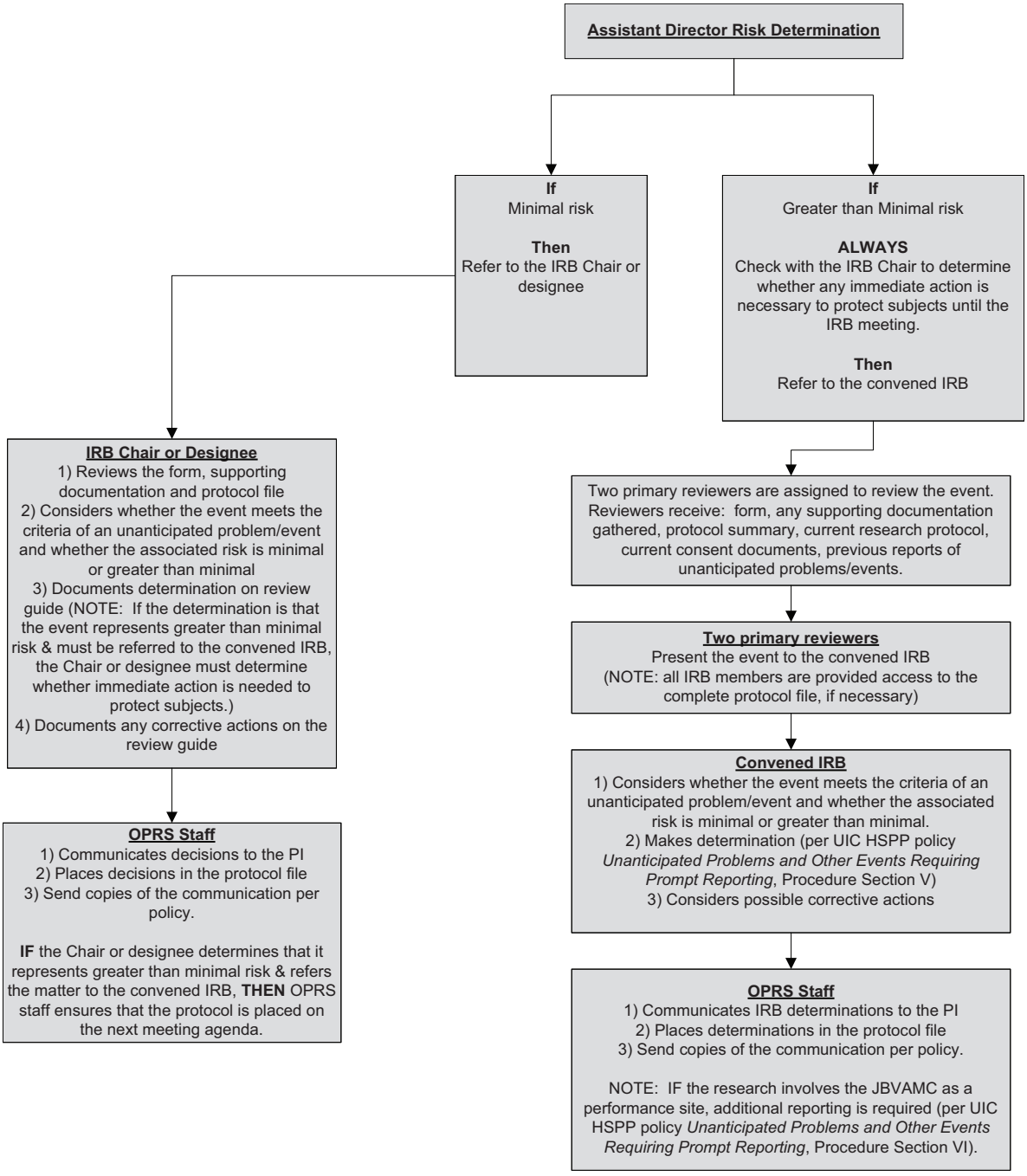
Chart B



Tip Sheet 17 • Prompt Reporting Process and Definition of Terms

What is the appropriate procedure for Prompt Reporting?

Chart C



Tip Sheet 17 • Prompt Reporting Process and Definition of Terms

What is the appropriate procedure for Prompt Reporting?

Prompt Reporting Defintion of Terms	
Unanticipated problems involving risks to subjects or others (i.e., unanticipated problem)	Refers to a problem, event or information item that is not expected, given the nature of the research procedures and the subject population being studied; and suggests that the research places subjects or others at greater harm related to the research than was previously known or recognized.
Unanticipated	means that the specificity, severity or frequency of the event is not expected based on (a) information contained in the protocol, investigator's brochure, informed consent document, drug or device product information or other research materials; and (b) the characteristics of the subjects, including natural progression of any underlying diseases.
Related	means that the event is more likely than not to have been caused by the procedures associated with the research.
Greater harm	means the research causes harm (including physical, psychological, economic or social harm) to subjects or others (e.g., family members, co-workers, study staff) or places them at a greater risk of harm than was previously known or recognized.
Adverse events	are untoward physical, psychological, social or economic events in a research subject which occurs during the study having been absent at baseline or, if present at baseline, appears to worsen. The event may be any unfavorable outcome, including abnormal laboratory result, symptom, disease or injury. Adverse events may be expected or unexpected, may not be caused by the research, and may be serious or not. Only a small fraction of adverse events qualify as unanticipated problems (unanticipated, related, and involve risk to subjects or other) and require reporting to the IRB.
Serious adverse events	include those resulting in death, life-threatening injury, hospitalization or prolongation of hospitalization, persistent or significant disability, or a congenital anomaly or birth defect. Events not meeting the above criteria but requiring intervention to prevent one of these outcomes are also considered serious adverse events.

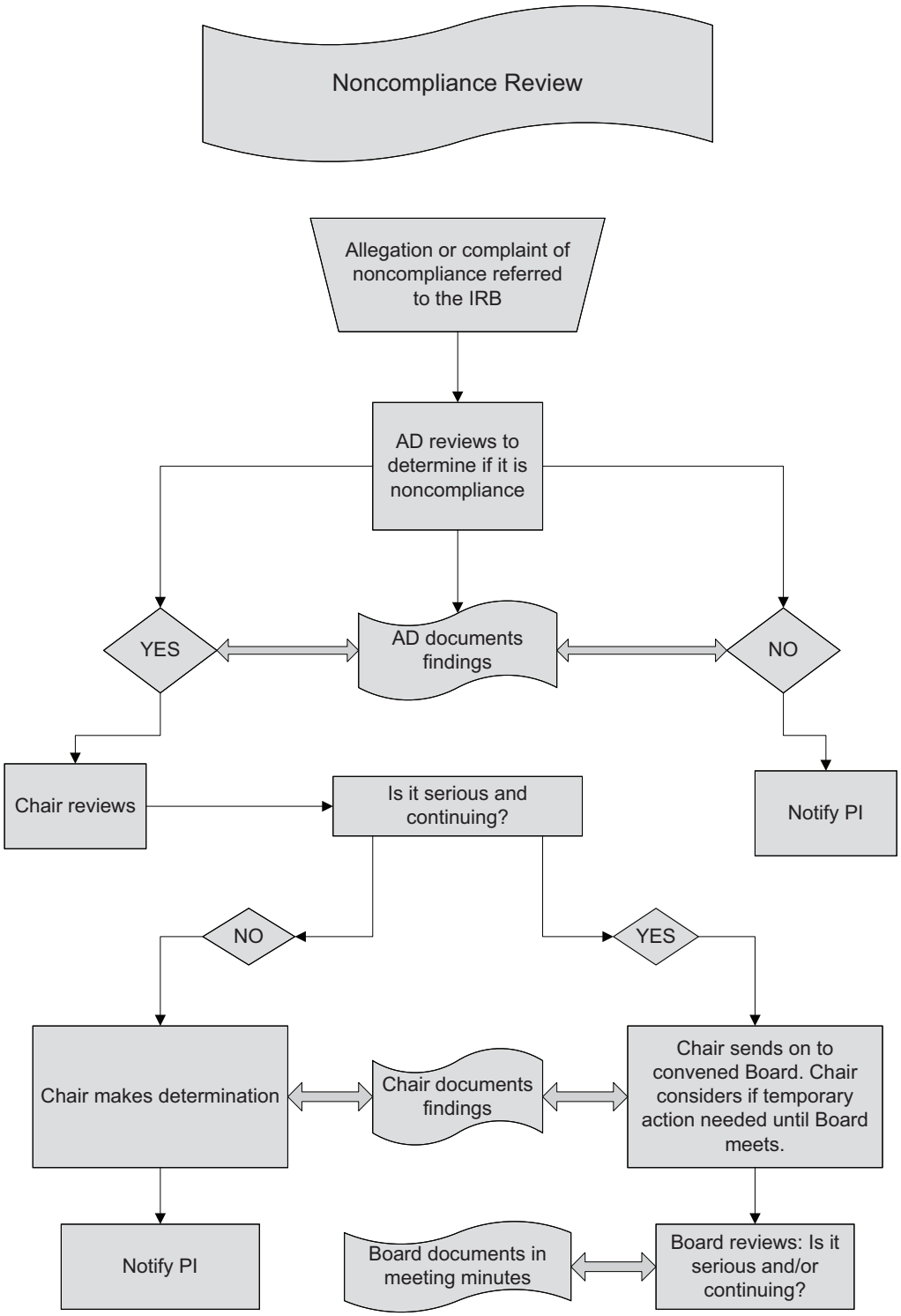
Tip Sheet 17 • Prompt Reporting Process and Definition of Terms

What is the appropriate procedure for Prompt Reporting?

Unanticipated Adverse Device Effects	are any serious adverse effect on health or safety or any life-threatening problem or death caused by or associated with a device used during human subjects research if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
Protocol violations	are any unplanned and unintentional deviations or variances in the conduct of the research that are implemented prior to IRB approval.
Internal adverse events	are those occurring at UIC, JBVAMC or other sites where the UIC IRB has oversight responsibility for the research (e.g., UIC is the primary site or coordinating center for a multi-center trial, UIC IRB is IRB of record).
External adverse events	are those occurring at non-UIC sites where the UIC IRB has no oversight responsibilities. These are typically reported to investigators at other sites by sponsors as IND safety or Medwatch reports, and do not require prompt reporting unless documentation is provided identifying them as unanticipated problems (i.e. unanticipated, related and increase risk of harm).
Non-compliance	refers to conducting research involving human subjects in a manner that intentionally or unintentionally fails to comply with federal or state regulations, VHA Handbook 1200.5, or the requirements or determinations of the IRB. Examples include, but are not limited to, initiating research prior to IRB approval, deliberate or repeated protocol violations, using inadequate procedures for informed consent, failing to meet education and training requirements and lapses in IRB approval.
Administrative hold	is a voluntary action by an investigator or sponsor to temporarily or permanently stop some or all research activities as a modification to approved research. Administrative holds are not considered suspensions or terminations Although the investigator may discuss this action beforehand with the IRB, IRB chair, or OPRS Director or Assistant Director, the hold must be initiated voluntarily by the investigator and must not be used to avoid IRB mandated suspension or termination or reporting requirements. During administrative hold, the research remains subject to continuing review and requirements for reporting noncompliance and unanticipated problems involving risks to subjects or others.

Tip Sheet 18 • Non-Compliance

What is the appropriate procedure for a non-compliance determination?



Tip Sheet 19 • VA Tissue Banking

http://www.research.va.gov/programs/tissue_banking/default.cfm

FAQ: Banking of Human Biological Specimens for Research

Q: How do you define human biological specimens?

A: A human biological specimen is any material derived from a human subject—such as blood, urine, tissues, organs, hair, nail clippings, or any other cells or fluids—whether collected for research purposes or as residual specimens from diagnostic, therapeutic, or surgical procedures.

Q: When are specimens considered to be banked specimens?

A: Biological specimens collected and stored for future research purposes that are beyond the scope of work described in the original protocol and informed consent or those collected under a protocol designed for banking of specimens are considered banked biological specimens.

Q: Is all storage of human biological specimens considered banking?

A: Human biological specimens collected under a VA-approved protocol are not considered to be "banked" specimens if they are used for only the specific purposes defined in the protocol and are destroyed either when the specific testing/use is completed or at the end of the protocol.

If the specimens are sent to a non-VA institution for testing as defined in the protocol, once the specific analyses are performed, the remainder of the specimens must be destroyed or returned to the VA for destruction. If the specimens are destroyed at another institution, that institution must certify the destruction of the specimens in writing.

Important Notes:

- If the protocol is 5 years or longer and the specimens are stored off-site at a non-profit institution until the end of the protocol, then the investigator must obtain a waiver from ORD.
- If the specimens are stored off-site at a non-academic, for-profit institution for greater than 3 months while awaiting analysis, a waiver must be obtained from ORD.

Q: Is banking of bacteria or fungus samples obtained from human specimens considered tissue banking?

A: No, not as long as the human material has been removed.

Tip Sheet 19 • VA Tissue Banking

http://www.research.va.gov/programs/tissue_banking/default.cfm

Q: Does a VA investigator need approval from the Office of Research and Development (ORD) to establish a tissue bank on a VA campus?

A: No. A tissue bank established at a VA site by a VA-paid investigator does not require ORD approval. However, the ACOS/R should maintain records of all tissue banks within the facility.

Q: Does a VA investigator need approval to bank biological specimens collected from subjects at the VA Medical Center at his/her University affiliate?

A: Yes. If the specimens are banked at a site that is not on the VA campus, ORD approval is required.

Q: I am a Without Compensation (WOC) investigator at the VA. May I apply for a waiver for an off-site tissue bank or storage site?

A. Yes. If the PI on the study is WOC they may apply for a waiver, but only if they have a VA investigator, either part-time or full-time, take responsibility for the samples in the bank or at the storage site. The VA investigator needs to be located at the specific VA site that the application originates from. The VA investigator taking responsibility needs to send us a signed letter/memo indicating that they are taking responsibility for the samples on behalf of the WOC investigator for the study in question. The VA investigator does not need to be listed on the informed consent or protocol.

Q: My colleague received approval to bank specimens at off-site tissue bank XYZ. Do I need ORD approval to bank specimens there?

A: Off-site tissue banks are approved on a per protocol basis (with the exception of some NCI protocols listed in the answer to the next questions), so unless you are banking specimens for the same protocol as your colleague, you need ORD approval.

Q: Where can I find a list of VA-approved off-site tissue banks?

A: Tissue banks approved for multi-site protocols are listed below. This list is also posted on the VA R&D website.

Tip Sheet 19 • VA Tissue Banking

http://www.research.va.gov/programs/tissue_banking/default.cfm

The following banks are approved ONLY for the protocol listed:

Protocol	Protocol Acronym	Tissue Bank Name and Location
Action to Control Cardiovascular Risk in Diabetes	ACCORD	Northwest Lipid Metabolism and Diabetes Research Laboratories, Seattle, WA
Chronic Renal Insufficiency Cohort	CRIC	CRIC Study Central Lab & Repository, University of Pennsylvania, Philadelphia, PA
Hepatitis C Long Term Treatment Against Cirrhosis	HALT-C	SeraCare (formerly BBI Biotech), Gaithersburg, MD
Alzheimer's Disease Neuroimaging Initiative	ADNI	National Cell Repository for Alzheimer's Disease (NCRAD), Indianapolis, IN
Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglyceride and Impact on Global Health Outcomes	AIM-HIGH	Northwest Lipid Research Laboratories, University of Washington, Seattle, WA
Lung Tissue Research Consortium	LTRC	Tissue Processing Distribution Center-Tissue Core Lab, University of Colorado Health Sciences Center, Denver, CO
Idiosyncratic Liver Injury Associated with Drugs: A Retrospective Study	DILIN-ILIAD	NIDDK Genetics Repository (Rutgers University Cell and DNA Repository)
A Multi-Center Longitudinal Study of Drug- and CAMInduced Liver Injury	DILIN-CAM	NIDDK Genetics Repository (Rutgers University Cell and DNA Repository)
Action for Health in Diabetes	Look AHEAD	Look AHEAD Central Laboratory, University of Washington, Seattle, WA
Diabetes Prevention Program/Diabetes Prevention Program Outcomes Study	DPP/DPPOS	DPP/DPPOS Central Laboratory, University of Washington, Seattle, WA
Genetics of Endophenotypes and Schizophrenia	COGS	Rutgers University Cell and DNA Repository, Piscataway, NJ

Tip Sheet 19 • VA Tissue Banking

http://www.research.va.gov/programs/tissue_banking/default.cfm

In addition, as a result of a letter of understanding with the National Cancer Institute (NCI), the following NCI-sponsored cooperative tissue banks, are designated as VA-approved if they are used for one of their protocols (for example, the SWOG-supported tissue bank can be used for SWOG protocols without ORD approval):

Clinical Trials Cooperative Groups Tissue Resources, which include

American College of Surgeons Oncology Group (ACOSOG)
Cancer and Leukemia Group B (CALGB)
Eastern Cooperative Oncology Group (ECOG)
Gynecologic Oncology Group (GOG)
North Central Cancer Treatment Group (NCCTG)
National Surgical Adjuvant Breast and Bowel Project (NSABP)
Radiation Therapy Oncology Group (RTOG)
Southwest Oncology Group (SWOG)
Cooperative Breast Cancer Tissue Resource
Cooperative Human Tissue Network
Gynecologic Oncology Group Tissue Network
Cancer Prevention Network
National Cancer Institute of Canada Clinical Trials Group (NCIC CTG)

Q: How do I apply for approval to bank or store biological specimens off-site?

A: **(Non-profit institution Application) Complete VA FORM 10-0436**
(http://www.va.gov/vaforms/medical/pdf/vha-10-0436-fill.pdf)
(For-profit institution Application) Complete VA FORM 10-0474
(http://vaww.va.gov/vaforms/medical/pdf/10-0474-fill.pdf)

The additional information requested on both applications can be scanned and attached to the pdf, which can be e-mailed to Marilyn Mason (offsite.tissuebanking@va.gov). Alternatively, the form and requested information can be mailed to the address given on the form. Please note that we do prefer you to email the documents. Please make sure that you send us the following documents that are listed on both applications. We cannot review your application until we receive the complete package.

- Research protocol
- Tissue bank manual or SOPs (if the bank in question has no manual or SOP's you can access the **Tissue Bank Operations Sheet** on the website)
- VA consent form
- HIPAA authorization

Tip Sheet 19 • VA Tissue Banking

http://www.research.va.gov/programs/tissue_banking/default.cfm

Q: How long does it take for ORD to process the application?

A: You will generally receive a memo within 2 weeks. Frequently, the memo will list issues found with the application, consent form, etc. and you will need to submit revisions.

Q: How difficult is it to get an application approved?

A: Most applications are eventually approved, but several revisions may be required. The most frequent problem is that required elements are missing from the informed consent and/or HIPAA authorization.

Q: Is there a list of elements that must be included in an informed consent when the protocol includes tissue banking?

A: Yes, they are posted on the VA website. There is a guidance document for both nonprofit and for-profit sponsored studies.

Q: Does the informed consent need to narrowly specify the future uses of the banked specimens? (Non-profits only)

A: No, the statement about future uses does not have to be very specific. If it is not specific, in the consent form or during the consent process, the PI should explain what such phrases as "related diseases" or "unspecified research" means for the use of the sample and the impact on the subject.

Q: Your tissue banking application requests a copy of the informed consent. Can I send it to you before sending it to the IRB for approval?

A: Yes, we would encourage you to do that. Often elements are missing, and we can point this out before you request IRB review. In addition, we can provide approval of your application that is contingent on IRB approval of the consent form. The approval of your application would also be contingent on the final study approval by the IRB committee and R&D committee, or ACOS of R&D.

Q: Why do we need the SOP's for the tissue bank or storage facility? What if we don't have them?

A: When we request to see the SOP's of the tissue bank or storage facility, this is to make sure our veteran's specimens are safeguarded. We do not need to know how tubes will be shipped or processed, but we do want to know if there is limited access to the specimens and power back-up for the storage units. If you don't have banking SOP's you can access the **Tissue Banking Operations Sheet** on the website, which can be saved and filled out using Adobe Reader. This form asks questions about specimen storage, facility security, and sample re-distribution. **Please note:** if your study is sponsored by a for-profit, the facility that is housing the specimens should have SOP's or a laboratory manual.

Tip Sheet 19 • VA Tissue Banking

http://www.research.va.gov/programs/tissue_banking/default.cfm

Q: I have specimens that were collected for a protocol that will soon end. Can I use them for a different protocol or test them for something (protein, gene, etc.) not in the original protocol?

A: If banking was not included in the original protocol and informed consent, then in order to use the specimens, you would need to re-consent the patients, or an IRB would need to waive consent, if applicable. If approval is obtained from subjects or the IRB waives consent, the samples would be considered banked samples. All new uses of the samples would have to be approved by the IRB and R&D Committees. If approval is not obtained, then the samples would have to be destroyed.

Q: Our pathology lab has paraffin-embedded specimens that it plans to destroy. Can we use the specimens for research, including genetic testing?

A: Your IRB must make that determination. Please note: clinical samples may NOT be transferred to a commercial (for-profit) entity for research purposes.

Q: Can we bank DNA/blood at a for-profit sponsor's site?

A: Currently, we are not permitting off-site tissue banking at for-profit entities, with the exception of NIH-sponsored banks, such as those at Coriell and ATCC. However, specimens may be stored at a commercial sponsor's site for up to 3 months while waiting for analyses/tests specified in the protocol to be performed. If the analyses/tests cannot be completed within the 3-month limit, a waiver must be obtained from ORD. *This waiver will allow specimens to be stored for up to 1 year past study completion date.*

Q: I am applying for a waiver and the study is sponsored by a for-profit company, but the protocol involved includes many study sites, not just VA. Is it possible to have the protocol document amended in order to incorporate specimen storage elements if ORD determines that information to be lacking?

A: Even if the protocol covers many study sites (including non-VA) an amendment can be included, and only refer to VA subjects that are enrolled/enrolling. We have had many sites request that the sponsor amend the protocol in order to incorporate details about specimen storage. We do not usually approve the study if these changes cannot be made.

Q: If I want to store specimens off-site for a multi-site clinical trial where several VA's are participating, how do I know that one of the other sites has not submitted an application for an off-site waiver? (For-profits only)

A: If you are not sure what other VA sites are involved, or have no communication with them, you can contact us anytime in order to make an inquiry. For a multi-site clinical trial study we usually accept one application from one site. If the waiver is approved we then send out a contingent approval which would

http://www.research.va.gov/programs/tissue_banking/default.cfm

apply to any other sites involved. Please do not assume that one of the other sites has submitted an application. If you have any hesitation, please contact us. If another site has already submitted, but you would like for us to look over your individual informed consent or HIPAA documents, we are more than willing to review them.

Q: With the new ORO guidance on VA sensitive information, and specifically the statement, "Thus, with a valid HIPAA authorization (or IRB approved waiver of authorization), the subjects' PHI stored on the affiliate's servers not considered "VA sensitive information" under VA Handbook 6500 because the data no longer belongs to the VA. According to OGC a VA CIO waiver is not required under these circumstances," do I need the database, that may contain patient identifiers, to be FIPS 140-2 encrypted?

A: If you're database is housed on the affiliate's server it does not need to be FIPS 140-2 encrypted as long as the HIPAA authorization is adequate (refer to VHA Handbook 1605.1, section 14 "Authorization Requirements"). If your study was initiated pre- HIPAA the database does not need to be encrypted as long as the consent form states that data will be stored. We will make this determination.

Q: You have an agreement in place with NCI regarding the use of tissue banks that they sponsor. What about other NIH Institutes?

A: Each NIH Institute sets its own policies regarding the repositories it sponsors, and our only agreement to date is with NCI.

Q: I am a VA-paid investigator and would like to bank blood for a study, but our VA Medical Center does not have the facilities to do that. Is there a VA-approved tissue bank that I can use?

A: You may bank samples at any VA Medical Center that has an established tissue bank. Alternatively, you could also use the Massachusetts Veterans Epidemiology Research and Information Center (MAVERIC) core laboratory at the Boston VA. It serves as the Cooperative Studies Program (CSP) Genetic Tissue Core Laboratory. The laboratory provides both local and national VA researchers a convenient, high-quality, low-cost mechanism to include biological specimen handling, storage and analysis in clinical studies. Laboratory capabilities include: coordination of collection, processing, shipment, and storage of serum, plasma, buffy coats and other biological specimens; extraction of DNA from blood, tissue, or serum buffy coat; extraction of RNA; and genotyping. See http://www.csp.research.va.gov/boston.cfm for contact information.

Tip Sheet 20 • VA Tissue Banking
Approved Tissue Banks

http://www.research.va.gov/programs/tissue_banking/approved.cfm

Protocol	Protocol Acronym	Tissue Bank Name and Location
Action to Control Cardiovascular Risk in Diabetes	ACCORD	Northwest Lipid Metabolism and Diabetes Research Laboratories, Seattle, WA
Chronic Renal Insufficiency Cohort	CRIC	CRIC Study Central Lab & Repository, University of Pennsylvania, Philadelphia, PA
Hepatitis C Long Term Treatment Against Cirrhosis	HALT-C	SeraCare (formerly BBI Biotech), Gaithersburg, MD
Alzheimer's Disease Neuroimaging Initiative	ADNI	National Cell Repository for Alzheimer's Disease (NCRAD), Indianapolis, IN
Atherothrombosis Intervention in Metabolic Syndrome with Low HDL/High Triglyceride and Impact on Global Health Outcomes	AIM-HIGH	Northwest Lipid Research Laboratories, University of Washington, Seattle, WA
Lung Tissue Research Consortium	LTRC	Tissue Processing Distribution Center-Tissue Core Lab, University of Colorado Health Sciences Center, Denver, CO
Idiosyncratic Liver Injury Associated with Drugs: A Retrospective Study	DILIN-ILIAD	NIDDK Genetics Repository (Rutgers University Cell and DNA Repository)
A Multi-Center Longitudinal Study of Drug- and CAMInduced Liver Injury	DILIN-CAM	NIDDK Genetics Repository (Rutgers University Cell and DNA Repository)
Action for Health in Diabetes	Look AHEAD	Look AHEAD Central Laboratory, University of Washington, Seattle, WA
Diabetes Prevention Program/Diabetes Prevention Program Outcomes Study	DPP/DPPOS	DPP/DPPOS Central Laboratory, University of Washington, Seattle, WA
Genetics of Endophenotypes and Schizophrenia	COGS	Rutgers University Cell and DNA Repository, Piscataway, NJ

Tip Sheet 20 • VA Tissue Banking
Approved Tissue Banks

http://www.research.va.gov/programs/tissue_banking/approved.cfm

In addition, as a result of a letter of understanding with the National Cancer Institute (NCI), the following NCI-sponsored cooperative tissue banks, are designated as VA approved if they are used for one of their protocols (for example, the SWOG-supported tissue bank can be used for SWOG protocols without ORD approval):

Clinical Trials Cooperative Groups Tissue Resources, which include:

- American College of Surgeons Oncology Group (ACOSOG)
- Cancer and Leukemia Group B (CALGB)
- Eastern Cooperative Oncology Group (ECOG)
- Gynecologic Oncology Group (GOG)
- North Central Cancer Treatment Group (NCCTG)
- National Surgical Adjuvant Breast and Bowel Project (NSABP)
- Radiation Therapy Oncology Group (RTOG)
- Southwest Oncology Group (SWOG)
- Cooperative Breast Cancer Tissue Resource
- Cooperative Human Tissue Network
- Gynecologic Oncology Group Tissue Network
- Cancer Prevention Network
- National Cancer Institute of Canada Clinical Trials Group (NCIC CTG)

Tip Sheet 21 • VA Tissue Banking
Informed Consent

The informed consent under which the specimen was collected must meet all the requirements in Appendix C of VHA Handbook 1200.05 "Requirements for the Protection of Human Subjects in Research." In addition, the informed consent must clearly address the following:

The types of specimens that will be stored and the name and location of the biorepository/tissue bank where they will be stored	Example 1: Your blood and DNA samples will be stored at the National Cell Repository for Alzheimer's Disease (NCRAD) in Indianapolis, IN.
	Example 2: Your DNA will be stored at the Rutgers University Cell and DNA Repository in Piscataway, New Jersey.
The types of future research that the sample will be used for	Example 1: Your DNA and serum will be stored for genetic testing. Genetic testing will be restricted to testing for genes related to dementia.
	Example 2: Your blood samples will be used for studies of any major disease or health condition, including genetic studies.
	Example 3: Your samples will be used for research on Alzheimer's disease and related diseases.
	Example 4: see Example 3 in the next section.
If the specimen will be shared with other researchers for approved research protocols	Example 1: The National Institute on Aging (NIA), a component on the National Institutes of Health (NIH), will make your DNA and clinical data available to other qualified scientists.
	Example 2: Your blood will be shared with other qualified researchers at the Bronx VAMC.
	Example 3: If you give permission, samples may be shared with other research laboratories studying the genetics of type 2 diabetes and the development of heart and blood vessel diseases, other major disease, health conditions, or risk factors.
	__I agree to allow my genetic sample to be studied for genes related to any major disease or health condition or risk factor.
	__I agree to allow my genetic sample to be studied only for genes related to diabetes, blood pressure, blood cholesterol abnormalities, heart disease, or other risk factors for heart disease or for diabetes.
	__I agree to allow my genetic samples to be used only for this study.

Tip Sheet 21 • VA Tissue Banking
Informed Consent

The informed consent under which the specimen was collected must meet all the requirements in Appendix C of VHA Handbook 1200.05 "Requirements for the Protection of Human Subjects in Research." In addition, the informed consent must clearly address the following:

The length of time the specimen will be stored	Example 1: Your samples will be stored for 15 years and then destroyed.
	Example 2: Your samples will be stored until none is left.
	Example 3: Your samples will be stored indefinitely.
If the specimen will be labeled with a code that doesn't contain any personal identifiers (i.e., protected health information as defined by HIPAA) and if the subject's clinical data will be linked to the specimen	Example 1: The sample and your clinical data will be assigned a code that does not contain your name, initials, SSN, date of birth, or other unique identifiers.
	Example 2: All identifiable information about you will be removed from the research specimen. Your sample and data will be identified by a code.
When and under what conditions research results will be conveyed to the subject, the subject's family, or the subject's physician	Note: Laboratories that test human specimens cannot report patient specific results for the diagnosis, prevention, or treatment of any disease or impairment of, or the assessment of the health of individual patients unless the laboratory is Clinical Laboratory Improvement Amendments of 1988 (CLIA) certified.
	Example 1: These tests are being done for research purposes only; you and your doctor will not be informed of the results.
	Example 2: Reports about research done with your samples will not be given to your or your doctor because they will not have any direct clinical benefit to you at this time.
	Example 3: Because these results have no clear meaning for you at this time, we will not report the results of the XYZ testing to you. XYZ testing is not a proven marker for Alzheimer's disease.

Tip Sheet 21 • VA Tissue Banking
Informed Consent

The informed consent under which the specimen was collected must meet all the requirements in Appendix C of VHA Handbook 1200.05 "Requirements for the Protection of Human Subjects in Research." In addition, the informed consent must clearly address the following:

The steps necessary for the subject to withdraw from the study and any future studies in which the specimens may be used. The consent must indicate what will occur to the data collected to that point and that the specimen and the code that links the subject's clinical data to the specimen will be destroyed	Example 1: You may withdraw your consent at any time. Please notify Dr. XXX at <phone number> to withdraw your consent. Your DNA, plasma, and all links to your clinical data and any data obtained from this research study will be destroyed.
	Example 2: You may withdraw your consent at any time. Please notify Dr. XXX at <phone number> to withdraw your consent. Your DNA, plasma, and all links to your clinical data stored in the repository will be destroyed. However, any de-identified samples that have been shared with other researchers cannot be destroyed.
	Example 3: You may ask the researchers to stop using your health information at any time. Contact Dr. XXX at <phone number>. The research team will continue to use any information that they have already collected to ensure the integrity of the research. However, no new information will be collected from you.
Disclose any potential commercial benefits and if the subject will receive money or other benefits	Example 1: Your specimens will be used for research and such use may result in inventions or discoveries that could become the basis for new products or diagnostic or therapeutic agents. In some instances, these inventions and discoveries may be of potential commercial value. You will not receive any money or other benefits derived from any commercial or other products that may be developed from the use of the specimens.
	Example 2: The use of your sample may result in inventions or discoveries that could become the basis for new procedures of diagnostic or therapeutic agents. In some instances, these inventions and discoveries may be of potential commercial value and may be patented and licensed. Commercially available products may be developed from these samples. There are no plans to share any of these profits with you.
Disclose any intent to perform genetic tests	Example 1: Genetic tests will be confined to testing for genes relating to liver diseases, including hepatitis and cancer.
	Example 2: Genetic material (DNA) will be isolated from the blood or tissue sample that you donate. It will be used to test for genes relating to prostate cancer.

Tip Sheet 21 • VA Tissue Banking
Informed Consent

The informed consent under which the specimen was collected must meet all the requirements in Appendix C of VHA Handbook 1200.05 "Requirements for the Protection of Human Subjects in Research." In addition, the informed consent must clearly address the following:

Disclose any potential risks to the subject or the subject's family. Potential risks may include breach of confidentiality, which may lead to discrimination in the areas of employment, insurability, social stigmatization, or psychological stress caused by disclosure of adverse information to the subject or the subject's family	Example 1: It is theoretically possible that genetic information about you could lead to denial of insurance or employment. Therefore, information about you will not be given to other family members (unless you give permission, or unless you need a representative at a later date), insurance companies, or employers.
	Example 2: The study results might be stressful to you if we were to find that you carry a gene for a neurological disease.
	Example 3: We will make every effort to protect your confidentiality and make sure that you identity does not become known. All written information will be stored in a locked file cabinet, and electronic data will be encrypted. A limited number of staff members will have access to the data. However, there is a slight risk of a breach of security.

Tip Sheet 22 • VA Consent Language

Privacy and Confidentiality	• "The only people who will know that you are a research subject are members of the research team, individuals who may have access to your medical record and/or informed consent document due to their job function at the JBVAMC, and, if appropriate, your physicians and nurses. No information about you, or provided by you during the research, will be disclosed to others without your written permission, except: if necessary to protect your rights or welfare (for example, if you are injured and need emergency care);or when the UIC/NU/JBVAMC Institutional Review Board monitors the research or consent process; or when the JBVAMC research and Development Committee monitors the research or consent process, or when the Government Accounting Office (GAO), the Office for Human Research Protections (OHRP) or other governmental regulatory agencies monitor the research; or if required by law."
Injury Language	• If you are injured or harmed from taking part in this research study, medical care (emergency or immediate non-emergency) for the injury will be provided to you at no cost by the VA. The VA has not set aside funds for other payments if research subjects are injured or harmed. You are not giving up any legal rights or released the VA or its agents from liability for negligence by signing this form.
Contact Language	• "In the event of a research-related injury or if you experience an adverse event, please immediately contact Dr. (insert name) at (XXX) XXX-XXXX) during the day and (XXX) XXX-XXXX) after business hours. If you need emergency hospitalization in a private hospital have a family member or friend contact Dr. (insert name) so that the VA can coordinate your care and any related costs with the private hospital. The VA will pay the costs of necessary care related to the research.
Cost Language	• Some veterans pay co-payments for medical care and services provided by the VA. These co-payment requirements will continue to apply to standard medical care and services provided by the VA that are not part of this study. You will be expected to pay these costs according to your usual method of payment. Except for required co-payments, there are no additional costs to you for being part of this study.
Required Signature Lines	• Subject • Subject's legally authorized representative (only applicable when required and approved by the IRB) • Witness • Person obtaining consent

Tip Sheet 22 • VA Consent Language

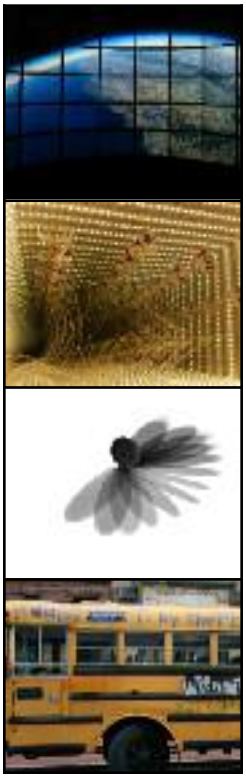
Informed Consent - General	• Type of specimens that will be stored and the name and location of tissue bank where they will be stored; • Types of future research the sample will be used for and allow the subject the choice of how the specimen will be used (e.g., any research, genetic analysis, research related to related to specific areas); • If specimen will be shared with other researchers for approved research protocols; • Length of time specimen will be stored (e.g., 5 years and then destroyed; indefinitely); • How specimen will be labeled, whether the code identifying the sample will contain any personal information and if the subject's clinical data will be linked to specimen; • If research results will be conveyed to the subject, subject's family, or subject's physician; • Disclose any potential commercial benefits and if the subjects will receive money or other benefits; • Whether the subject will be re-contacted after the original study is completed; AND • Steps necessary for the subject to withdraw from the study and any future studies in which the specimens may be used. The consent must indicate what will occur to the data collected to that point and that the specimen and code that links the subject's clinical data to the specimen.
If the research involves genetic testing, the informed consent must address the following	• The intent to perform genetic testing and a description of the testing (e.g., genes related to epilepsy); and • Potential risks to the subject or subject's family (e.g., breach of confidentiality, which may lead to to discrimination in the areas of employment, insurability, or social stigmatization, or psychological stress caused by disclosure of adverse information to the subject or subject's family).

Tip Sheet 23 • Key Definitions Glossary

Please refer to the UIC OPRS glossary on the Internet for a comprehensive glossary

Minimal Risk	The probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.
Minimal Risk - Prisoners	The probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. Note: This definition of minimal risk differs from that in 45 CFR 46 Subpart A by replacing "harm or discomfort" with "physical or psychological harm" and using "healthy person" as the reference point for the medical, dental or psychological examinations.
Vulnerable Populations	The UIC IRB ensures that additional safeguards are included in the research design to protect the rights and welfare of research subjects who have limited autonomy and are at risk for coercion and undue influence.

Cover Art



Plantary-Scale Data Rendering in
Autostereoscopic Virtual Reality -
Robert Kooima, Computer Science

Infinity Gliders - AnnMarie Cernoch, Art + Design

13 Hours at Once - Renata Graw, Graphic Design

Withoute Justice No Peace - Margaret Hagerman, Sociology

UIC OFFICE OF THE VICE CHANCELLOR FOR RESEARCH

Office for the Protection of Research Subjects
AOB 203, MC 672
1737 W. Polk Street
Chicago, IL 60612-7227
312-996-1711
uicirb@uic.edu
www.research.uic.edu/protocolreview/irb