

4. How to Apply for Review

4.1 The CPHS Process

The CPHS reviews a proposal first by assessing the risks and benefits of research participation. CPHS requires researchers to submit a University of Houston CPHS Application to Conduct Research Using Human Subjects. After determining that the research benefit outweighs the risks involved, the CPHS turns to the consent process to ensure that potential subjects are fully aware of the risks and benefits and that they participate in the project voluntarily. The consent is a key element in the review. The CPHS will also determine whether or not the scientific questions addressed in the protocol have adequate merit to justify the involvement of human subjects.

After reviewing all materials, the CPHS may opt to approve, table, or reject the application. The CPHS may require revisions in the protocol. After the investigator revises a project, the CPHS reviews the project again to see whether its concerns have been adequately addressed.

To fully protect subjects, the CPHS must approve a project before investigators start to work on it – even before they begin to recruit subjects, since recruitment strategies are part of the review. Although there are different types of review, many projects require “full” committee review. The initial full review will occur according to the published submission deadlines. All CPHS actions are communicated in writing to the investigator by the CPHS staff. If the investigator is a student, the letter is addressed to the investigator in the care of the faculty sponsor.

4.2 Primary Types of Review

The CPHS reviews research projects according to the risk to subject and at one of three levels defined in federal regulations:

- full convened CPHS review,
- expedited, CPHS review, and
- administrative review for exemption from full CPHS review.

The CPHS will determine the level of review.

4.3 Full Review

A project that involves greater than minimal risk or does not qualify for exempt/expedited review requires approval from a CPHS panel composed of members qualified to review research in that field. Research that requires full committee review includes:

- research that involves greater than minimal risk;
- non-exempt research that involves children or other vulnerable populations;
- research that involves experimental drugs or devices;
- research that involves invasive procedures; and
- research that involves deception.

Survey research that involves sensitive questions or information about sexual practices or illegal behavior is subject to full review, in keeping with federal guidelines. Additionally, any survey or interview that is

likely to be stressful for the subject requires full committee review. The CPHS administrator will make this determination.

The administrative staff screens all applications before they are assigned to an CPHS panel. *If incomplete, the application is returned to the investigator.* The CPHS reviews only complete applications (see 4.1). After review, the CPHS will act on the application. Possible committee decisions include:

- approved as submitted;
- approved with requests for minor changes;
- approved with contingencies (conditions that must be met before final approval is granted);
- deferred pending receipt of additional information or major revisions; or
- disapproved.

All non-exempt research is subject to continuing review at least annually [refer to 8.0 Continuing Review].

4.4 Expedited Review

To qualify for expedited review, a research project must be limited to the activities that are federally approved for expedited review and incur no more than minimal risk for participants, or be a minor change in previously approved research that involves no additional risk to the research subject.

The activities approved for expedited review are:

1. Clinical studies of drugs and medical devices, only when condition (a) or (b) is met. (a) research on drugs for which an investigational new drug application (21 CFR Part 312) is 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.); or (b) research on medical devices for which (i) an investigational device exemption application (21 CFR 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with cleared/approved labeling.
2. Collection of blood samples by finger stick, heel stick, ear stick or venipuncture as follows: (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 (b) from other adults and children (as defined by the HHS regulations as “persons who have not attained the legal age for consent to treatments or procedures involved in this research, under the applicable law of the jurisdiction in which the research will be conducted), 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.
3. Prospective collection of biological specimens for research purposes by noninvasive means. 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 a 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

scaping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

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.
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).
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.
8. Continuing review of research previously approved by the convened CPHS as follows: (a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or (b) where no subjects have been enrolled and no additional risks have been identified; or (c) where the remaining research activities are limited to data analysis.
9. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the CPHS has determined and documented at a convened meeting that the research involves no greater than minimal risk and additional risks have been identified.

The researcher must demonstrate in the application how the proposed project activities fall into one or more of these categories. To apply for expedited review, investigators complete the Application to Conduct Research using Human Subjects and indicate that they are requesting expedited review in the appropriate section.

The CPHS administrator will ensure that all of the elements essential for review, including consent forms and supporting documentation, have been submitted. The administrator will then forward the application for review and approval by either the CPHS subcommittee or the full committee, depending on the submission deadlines.

In accordance with 45 CFR 46.110(c), the applications approved under the expedited procedures by the subcommittee are reported to all members of the full committee. The full committee shall receive a copy of the minutes from the subcommittee meeting listing the protocols that were reviewed and the decision.

4.5 Administrative Review for Exempt Status

While research that involves only minimal risk to human subjects is sometimes exempt from full CPHS committee review, it is still subject to review. Investigators do not have the authority to determine whether research involving human subjects is exempt from full review [45 CFR 46.101(b) and (c)]. Researchers must file an application requesting that the CPHS determine exempt status for a project. Exemptions are approved for a specific research project conducted by specific investigators. Departments cannot receive blanket exemptions for unspecified research (e.g., surveys, public observations) to be conducted in the future.

OHRP offers the following chart to determine if research is eligible for exemption status:

Projects that involve contact with subjects may still qualify as exempt. In general, the federal guidelines for research on human subjects allow a project to be exempt from full review only if the research involves no risk to the subject and the procedures are limited to the following criteria:

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 (2) of this section, if: (i) the human subjects are elected or appointed 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.
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.

The application form is available from the Division of Research office or its web site. Copies of the written consent form should be filed with the application or justification for a waiver of written documentation should be provided. See 45 CFR 46.117.

The CPHS administrator will decide whether the project qualifies as exempt, and confirms the decision in writing. If the project does not qualify as exempt, it will be submitted to the appropriate committee based on the posted Submission Deadlines. Again, the investigator will be notified in writing.

Exemptions are approved for a maximum of five years after approval. To continue research after that time period, investigators must apply for another exemption.

4.6 Appeal of CPHS Determination

Investigators who have been required to make revisions in their applications or whose applications have been disapproved may request further information regarding its reasons from the CPHS or may ask the CPHS to reconsider its decision. Such requests must be made in writing and will be considered by the CPHS at the next convened meeting, if submitted according to the published deadline for submission of materials to the CPHS. At its discretion, the CPHS may invite investigators to meet with the CPHS or a subcommittee of the CPHS to collect additional information or to explain the reasons for its decision. The CPHS will provide investigators with a written explanation of its reasons or its decision upon reconsideration. The CPHS's decision will be final, and no further appeal can be made.

4.7 Application Forms and Original Signatures

All forms that an investigator must file with the CPHS to apply for review are available with specific instructions on the Web at www.research.uh.edu (then click on "human subjects"), or from the Office of Research Policies, Compliance and Committees. The RPCC staff can help researchers determine which application is appropriate for a project. The forms available are:

- Application to Conduct Research using Human Subjects
- Application for Revision to a Currently Approved Protocol
- Application for Renewal

A signature page provides space for the signature of the principal investigator and co-investigators. An original signature certifies that the investigator will be actively involved in the research project and has made a commitment to protect the research subjects according to the federal regulations and institutional policies. Faculty sponsors must sign all student research proposals. Department heads (or college deans) must sign all faculty, staff and student proposals. [Note: Signature from the department head (or college dean) is not required for applications requesting exempt approval.] Signatures must be original.

All other documents submitted to the CPHS (such as interim reports, requests for revisions, adverse events reports, renewal applications) also require original signatures. Staff signatures will not be accepted. The principal investigator remains ultimately responsible for the protection of subjects.

Finally, before submitting the application with original signatures, investigators must:

- retain a copy of all submitted materials for their own records; and
- attach the appropriate number of copies required:

for full CPHS review (CPHS – Committee 1) – original plus 9 copies of the application, appropriate consent documents, interview questions and/or questionnaires, and any additional information.

for full CPHS review (SSCPHS – Committee 2) – original plus 5 copies of the application, appropriate consent documents, interview questions and/or questionnaires, and any additional information.

for expedited review (both Committee 1 and 2) – original plus 2 copies of the application, appropriate consent documents, interview questions and/or questionnaires, and any additional information.

4.8 Preparing the Application

To submit a project to the CPHS for review, an investigator must complete the application form according to detailed instructions and enclose supporting material as required.

A fully complete application form will include:

- a) an up-to-date version of the appropriate application form (available at www.research.uh.edu);
- b) answers to **every** question on the form;
- c) appropriate attachments to the application;
- d) a lay abstract describing the purpose of the study;
- e) a description of the study population, criteria for inclusion/exclusion, the number of subjects, the process of identifying potential subjects, and any other plans related to the selection of subjects;
- f) a description of the tasks that subjects will be asked to perform;
- g) a full description of the anticipated risks and benefits of participating in the study;
- h) an explanation of how risks will be minimized;
- i) documentation of provisions to care for subjects in case of accident or injury (if applicable);
- j) a full description of procedures for maintaining confidentiality;
- k) a description of the process by which informed consent will be obtained from the appropriate individuals;
- l) documentation of any required approvals or applications for approval from other committees and/or from cooperating agencies;
- m) all supporting materials and documents, including protocol, interview schedules, solicitation letters, advertisements, and any survey instruments; and
- n) appropriate original signatures, including the faculty sponsor's signature for student research, and the department head/college dean (when applicable).

The application form will serve as background information for all future reviews of the study. For this reason, "see protocol" or "see attached" are not adequate responses to any application question. The application is designed to provide the CPHS with sufficient information about the proposed research activity to make the following determinations prior to approval:

- Risks to participants are minimized by using procedures that are consistent with sound research design and that do not unnecessarily expose them to risks.
- Risks are reasonable in relation to anticipated benefits, if any, to participants and the importance of knowledge that may reasonably be expected to result.
- Selection of subjects is equitable. In making this determination, the CPHS takes into account the purposes of the research and the setting in which the research will be conducted and is particularly cognizant of the special problems of research involving vulnerable populations, including children, prisoners, pregnant women, persons with impaired decision-making capabilities, and economically or educationally disadvantaged persons.
- Informed consent is sought from each prospective participant or the participant's legally authorized representative and is appropriately documented.
- When appropriate, the research plans make adequate provisions for monitoring the data collected to ensure the safety of participants.

- When appropriate, there are adequate provisions to protect the privacy of participants and confidentiality of the data.
- For participants who are likely to be vulnerable to coercion or undue influence, additional safeguards are included to protect their rights and welfare.

No form can address adequately the wide diversity of research at the University of Houston. Principal investigators should use the form to convey the nature and specifics of the project proposed and attach appendices as necessary.

4.9 Designating the Principal Investigator

The CPHS recognizes only one Principal Investigator (PI) for each project. The PI must be a faculty member, student or staff member at the University of Houston. On research conducted by students, a faculty member must serve as the sponsor and assume responsibility for exercising appropriate oversight of the student's research.

The PI, including the faculty sponsor in the case of students, must personally review and sign all applications, revisions, renewals, and other documentation submitted to the CPHS. The PI is responsible for identifying key personnel involved in the conduct of research, monitoring their activities, informing the CPHS of proposed changes, adverse events, and responding in a timely fashion to inquiries or requests from the CPHS.

All official correspondence is addressed to the PI. In the case of student researchers, correspondence is addressed to the student, care of the faculty sponsor. All correspondence is sent via campus mail.

Any change in the PI or in the PI's status that affects the project must be communicated to the CPHS. [See section 6.2 Making Changes to Research Protocols.]

4.10 Summary of Proposal: Rationale and Methods

Investigators must provide a summary of their proposed research in non-technical terms. For any risks associated with human research to be warranted, and hence, for research to be ethical, studies must have scholarly or scientific merit. Any study that does not have the potential to contribute to knowledge or that is fundamentally flawed in its methods cannot be approved by the CPHS. When research is not flawed, but could be strengthened in the opinion of CPHS members, the CPHS may provide recommendations to investigators that they may follow at their discretion.

Investigators should summarize the rationale for the research, including the research questions the study is intended to answer or the knowledge to be contributed by the study in the lay summary. This section should not be used to describe the methods in the proposed research.

Investigators must describe the nature of the intervention or interaction with potential participants or the nature of private information to be collected and analyzed. Both the general methodological tradition (e.g., qualitative versus quantitative) and specific methods (e.g., participant observation, interviews, surveys) should be described. The CPHS examines applications to ensure that the research methods are appropriate given the research rationale and questions.

The investigator must provide information on specific procedures, the nature and number of interventions or interactions with participants, and the analytical procedures. Researchers using participant observation or anthropological field work methods should be specific regarding where and among whom observations will be recorded and how they will identify themselves. The CPHS discourages covert participant observation in which the investigator conceals his or her identity as a researcher and will

require a clear justification for this approach. The investigator must demonstrate that the researcher could not be conducted overtly and that participants will not be harmed or exposed to undue risk.

4.11 Specifying the Number of Research Subjects

The application must specify the number of study subjects to be recruited and the number to participate, grouped by age, gender, and population diversity. Exceeding the recruitment limits approved by the CPHS is a violation of the protocol. The CPHS must give prior written approval for any increase in subjects. This can be done through a revision request to CPHS.

The CPHS is charged with the protection of human subjects from the earliest contact for possible recruitment. All subjects who go through the recruitment process screening must be accounted for, even if they fail or decline participation. When calculating the number of subjects in research design, please include a number large enough to account for this group.

If it is difficult to predict how many subjects will be eligible or be attracted to a study, the optimum number should be specified. Responses such as “don’t know” or “as many as we can recruit” to questions about the number of subjects are not acceptable.

Multicenter studies, in which data will be pooled and recruitment may vary, present a special problem for investigators. The application should provide information about the total picture, including both the number of subjects to be studied at the University of Houston or by University researchers and information on overall recruitment goals.

4.12 Women and Minorities in Study Populations

Research benefits and burdens should be distributed fairly. If an individual or group is denied access to a clinical trial that might be beneficial, or if some people are singled out to bear the burden of risks associated with a study, the requirement for fairness is not met.

In accordance with the policies of the National Institutes of Health, the CPHS requires applicants for federal funds to provide data regarding the subject populations by gender and minority group. Studies with the potential to address issues relevant to both genders must recruit both genders, and include minority groups in a study population wherever feasible. Researchers must justify the exclusion of any group of individuals. The CPHS makes exceptions if there is adequate scientific justification for exclusion, such as when a disease predominates in one gender or the focus of the research question is on a specific group.

4.13 Students or Employees as Research Subjects

Though the researcher must be careful to avoid potentially coercive behavior, the very nature of the relationship with the subject can create the appearance of coercion. For this reason, researchers should be aware of the potential for coercion that exists when a research subject is also a student, employee, colleague, or subordinate of the researcher. Therefore, researchers should avoid using their own students or employees as research subjects.

If there is sound scientific reason to include their own students, researchers should:

- ensure that students clearly understand that participation will not influence class standing, grades or other benefits under the control of the researcher.

- limit the use of extra credit points as a reward for participating; points should be used only when the research is closely tied to the course subject matter and should not raise a student's grade by a whole step (for example, from a B to an A). Students should be offered an alternative assignment of a non-research nature that entails the comparable level of time as the research activity. Students who participate in part, but not all of the research should be offered partial credit for participation according to the amount of time spent (an alternative assignment comparable in time must be offered to enable students to receive full credit).
- avoid using class time to recruit subjects or complete study instruments.

Researchers who select colleagues or subordinates as research subjects must be able to provide a rationale other than convenience for recruitment and must show that the recruitment method does not imply penalty or compromise by refusing to participate. Recruitment through bulletin board advertisements or by a third party is preferable.

A detailed description of **how** students and colleagues will be recruited and how coercion will be avoided must be included in the information submitted to the CPHS.

4.14 Children as Subjects

All research that involves minor subjects is subject to the application of 45 CFR 46 Subpart D. In all cases, inclusion or exclusion of children is reviewed for appropriateness as defined in the regulation.

In general, if research involves greater than minimal risk, children can be included in the study population only if there is direct personal benefit to the child. This restriction applies to research in both the health sciences and the social sciences. A research protocol that involves anything more than minimal risk and that offers no potential benefit to the subject cannot include children unless all conditions of 45 CFR 46.406 are met. Investigators claiming this provision in 45 CFR 46.406 should be prepared to provide justification.

4.15 Prisoners and Institutionalized Persons

All research that involves prisoners is subject to the application of 45 CFR 46 Subpart C. Prisoners and other institutionalized persons should neither bear an unfair share of the burden of participating in research nor should they be excluded from its benefits to the extent that voluntary participation is possible. Persons confined to institutions must not be selected as research subjects simply because they represent a convenient population to study.

The CPHS recognizes the special vulnerability of prisoners and other institutionalized persons who live under the supervision and formal authority of others. Prisons include jails, detention centers, and state and federal prisons. Institutions include psychiatric centers or mental hospitals, development centers for people with developmental disabilities, nursing homes, and similar facilities. The CPHS requires that research involving prisoners and institutionalized persons have risks commensurate with risks that would be accepted by non-institutionalized persons and that any possible advantages accruing to individuals are not of such magnitude that their ability to weigh the risks and benefits of the research, given an environment of limited choice, is impaired.

Procedures for selection of research participants in prisons should be fair and immune from the influence of prison authorities or prisoners. Investigators must ensure that participation of prisoners will not have bearing on decisions regarding parole, and prisoners will be informed of this. In view of violates of privacy that may occur in prisons, investigators must also take appropriate steps to maintain confidentiality in such settings.

To carry out its responsibilities under Subpart C, the CPHS must appoint an additional committee member or bring in an expert to guide the committee and who serves as a prisoner representative.

4.16 Persons who are Impaired in their Decision-Making

The ethical principle of respect for persons requires respect for the autonomy of individuals and special protections for those with diminished autonomy. Some persons may be limited in their competence to make informed decisions about their lives by virtue of mental, intellectual, or cognitive disabilities. Although investigators should be sensitive to the possibility that persons with disabilities may have limited capacity to consent to participating in research, they must not presume incompetence simply because a person has a disability diagnosis or label. Investigators must respect the autonomy of all persons unless there is clear evidence that they are incapable of decision-making.

For persons who have been formally adjudged incompetent and appointed a legal guardian, their guardians must provide consent for them to participate in research, with appropriate provisions for assent by the individual. Some adults who are incompetent to make major life decisions by virtue of a disability have not undergone a formal legal proceeding. In these instances, the CPHS may require that informed consent be provided by a parent, spouse, or other “next of kin” or by the assignment of an advocate or witness to oversee the consent process.

Persons with mental, intellectual, or cognitive disabilities must not be unilaterally excluded from participation in general research without justification.

4.17 Incentives for Participation

The CPHS reviews and approves incentives offered to subjects to participate in research. Subjects cannot receive payment to assume risk, but can receive compensation for the time and inconvenience involved in participation. Incentives may include monetary payment, course credit, gift certificates, toys or educational materials for children, and other items or services. Incentives must not be of such an amount as to result in undue influence or coercion on an individual’s decision to participate, especially in the case of persons who are poor. In addition, incentives must not be provided on a schedule that results in coercion or undue influence on an individual’s decision to continue participation. That is, incentives must not be withheld as a condition of an individual completing the research. If an individual withdraws early, payments or incentives may be prorated to reflect the time and inconvenience of the individual’s participation up until that point.

Payment to research participants must be arranged in a way that minimizes potential violations of privacy. For example, investigators should try to avoid linking subjects to participation in sponsored research involving sensitive topics (e.g., HIV and AIDS, drug use). In accordance with the University of Houston’s MAPP 05.02.04, UH employees participating as subjects in a research project must be paid through the payroll system via a PAR (Personnel Action Request).

The CPHS discourages lotteries for the payment of research participants, since these may create unrealistic expectations. Incentives for participation in research are not considered as benefits of the research and should not be reported as such on the CPHS application.

4.18 Advertising and Recruitment

Advertisements are part of the informed consent process and subject selection process. Copies of all advertisements, such as flyers, newspaper ads, radio and television announcements, URLs, bulletin board tear-offs, and posters, along with an explanation of other methods of recruiting subjects, must be submitted to the CPHS.

Advertisements should be submitted with the application or as soon as the principal investigator decides to use them. The content of advertisements should be limited to:

- names of the investigators and the university identified by name along with contact information,
- purpose of the research,
- general eligibility criteria, and
- straightforward and truthful descriptions of potential benefits and risks and payment (if applicable).

Advertisements should include the word “research” and should not claim, explicitly or implicitly, that the research is treatment or is superior to any current practice. Extravagant attention-getting devices such as extremely large, bold typefaces and dollar signs are prohibited. Statements of payment should not be in larger type than the rest of the ad. Advertisements should not pressure readers into participating. All recruitment materials should include the statement, “This project has been reviewed by the University of Houston Committee for the Protection of Human Subjects (713) 743-9204.”