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INTRODUCTION

The purpose of this Manual is to assist the faculty, staff, and students of The George Washington University (GWU), GWU Hospital, and Medical Faculty Associates (MFA) in fulfilling their duty to protect human subjects, i.e., individuals involved in research. All GWU, GWU Hospital, and MFA faculty, staff, and students participating in biomedical research involving human subjects or human subject material must be familiar with and abide by the guidelines set forth in this Manual. All GWU, GWU Hospital, and/or MFA faculty, staff, or students participating in social and/or behavioral human subject research must be familiar with and abide by the guidelines set forth the GWU Non-Medical IRB Manual, which can be accessed at http://www.gwumc.edu/research/human/nonmedical/nonmedical.htm.

The staff of the Office of Human Research (OHR), the office that provides administrative support to the GWU Committee on Human Research (CHR) Institutional Review Board (IRB) (hereinafter referred to as the GWU Medical IRB), sincerely hopes that this Manual sufficiently explains the policies, procedures, and considerations that the GWU Medical IRB undertakes when reviewing human subject research projects. Hopefully, this knowledge will give you, the reader, a better understanding of the GWU Medical IRB process.

In an effort to provide you with a better understanding of human subject research generally and the IRB process specifically we have **bolded and underlined** words of interest throughout the document. This **bold and underline** indicates that the word has been defined in Appendix A: Glossary of Terms, along with other human subject research-related words of interest.

If you should have any comments, concerns, or criticisms regarding this manual, please contact OHR by visiting the Office of Health Research, Compliance and Technology Transfer (OHRCTT), 712 Ross Hall (994-2995) or the OHR Staff, 613 Ross Hall (994-2715).
CHAPTER 1: HUMAN SUBJECT RESEARCH AT GWU

I. Authorities Governing Human Subject Research at GWU

A. Federal Regulations

The Department of Health and Human Services (HHS) has promulgated two separate sets of regulations for the protection of human subjects. The first set of federal regulations was drafted by the National Institutes of Health (NIH), Office of Protection from Research Risks (OPRR – subsequently renamed Office of Human Research Protections (OHRP)) and can be found at 45 CFR Part 46. These regulations are commonly referred to as the Common Rule for the Protection of Human Subjects (Common Rule). The Common Rule applies to all research involving human subjects that is conducted, supported, or otherwise subject to regulation by any Federal Department or Agency which takes appropriate administrative action to make the policy applicable to their department or agency research. In other words, the Common Rule applies to all human subject research involving: (1) federal funds; (2) other federal support (including, but not limited to, providing supplies, products, drugs, identifiable private information collected for research purposes, etc.) and/or (3) federal government employees, which is not otherwise exempt from the Common Rule. To date, numerous Federal Departments or Agencies, in addition to HHS, have adopted the Common Rule.

The second set of federal regulations was drafted by the Food and Drug Administration (FDA) and can be found at 21 CFR Part 50 and 56. 21 CFR Part 50 governs the informed consent process and 21 CFR Part 56 governs the general standards for Institutional Review Boards (IRBs). In short, these FDA regulations apply to all clinical investigations that are conducted to support applications for research or marketing permits for products regulated by FDA, including food and color additives, drugs/medical devices/biological products for human use, and electronic products. Please note that FDA has also promulgated regulations specific to the type of FDA regulated product under clinical investigation. For investigational drugs and biologics, you need to consult 21 CFR Part 312. For investigational devices, you need to refer to 21 CFR Part 812.

Fundamentally, both sets of regulations require that: (1) all research be reviewed by a peer review committee, called an IRB, prior to initiation of a research study involving human subjects; and (2) written informed consent be obtained prospectively from every potential human subject prior to taking part in a research study, unless waived or altered by the IRB in accordance with federal regulations.

For a summary of Significant Differences in FDA and HHS Regulations for Protection of Human Subjects go to http://www.fda.gov/oc/ohrt/irbs/appendixe.html or see Appendix B of this Manual.

In addition to the Common Rule and FDA regulations noted above, HHS has promulgated another set of regulations for the protection of certain information that is used or disclosed by certain individuals/entities for research purposes. This set of regulations is known as the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule regulations (the Privacy Rule). The Privacy Rule establishes, among other things, the conditions under which protected health information (PHI) may be used or disclosed by covered entities for research.
purposes. Please keep in mind that the Privacy Rule research related provisions are intended to protect the use or disclosure of PHI for research purposes whereas the Common Rule and FDA regulations are intended to protect the safety and welfare of human subjects. Thus, this is the reason why all non-exempt human subject research conducted at GWU is governed by the Common Rule and/or FDA regulations whereas only human subject research involving PHI is governed by HIPAA. For more information regarding HIPAA and research, please refer to Chapter 9 of this Manual.

B. Federal Guidelines

In addition to the federal regulations outlined above, NIH and FDA have promulgated guidelines for the conduct of certain types of research. Below is a representative list of NIH and FDA guidelines addressing various types of research considerations.

- International Conference on Harmonization (ICH) Guidelines, by FDA. [http://www.fda.gov/cder/guidance/959fnl.pdf](http://www.fda.gov/cder/guidance/959fnl.pdf). This document outlines the international ethical and scientific quality standard for designing, conducting, recording, and reporting trials that involve human subjects. This document is also referred to as the Good Clinical Practice (GCP) Guideline. Compliance with GCP assures that the rights, safety, and well being of trial subjects are protected, consistent with the principles that have their origin in the Declaration of Helsinki, and that the clinical trial data are credible. This ICH guidance provides a unified standard for the European Union, Japan, and the United States to facilitate the mutual acceptance of clinical data by the regulatory authorities in those jurisdictions. This guidance is applicable to clinical trials involving drug and biological products.
- NIH Guidelines for Inclusion of Children as Participants in Research Involving Human Subjects. [http://grants.nih.gov/grants/guide/notice-files/not98-024.html](http://grants.nih.gov/grants/guide/notice-files/not98-024.html). Pursuant to this guideline, children are to be included in all human subject research conducted or supported by NIH unless there are scientific or ethical reasons for not involving them. The goal of the guideline is to increase the participation of children in research so that adequate data is developed to support treatment modalities for diseases/conditions that affect adults as well as children.


C. Federalwide Assurance (FWA)

The GWU FWA is an agreement signed by GWU officials with OHRP, on behalf of the Secretary of HHS. The Assurance certifies the agreement of GWU that all non-exempt human subject research falling within the jurisdiction of the GWU IRB, including non-funded research, will be conducted in accordance with HHS regulations for the protection of human subjects. Thus, the GWU FWA applies to all human research conducted by GWU, GWU Hospital, and/or MFA faculty, staff, or students.

GWU has been issued FWA number 00005945 for a period of 3 years to expire on December 1, 2006. A copy of the FWA is available at www.gwumc.edu/research/FWA.htm. Noncompliance with the FWA can result in violations of the rights of human subjects. Additionally, noncompliance with the terms of the FWA can result in sanctions against the investigator(s) (principal or otherwise), GWU (to include GWU Hospital, and/or the MFA) or both.

Under the FWA, the GWU Medical IRB must review research even if it will be conducted at another institution with its own IRB. Where another IRB also has jurisdiction over the research, the principal investigator (PI) should inform the GWU Medical IRB of such information. The general rule for the GWU Medical IRB is to require submission of the project to the GWU Medical IRB first, with subsequent submission to the other institution’s IRB. The exception to this general rule pertains to studies that are conducted at Children’s National Medical Center (CNMC). Please refer to Chapter 2 regarding Cooperative Research Endeavors.

D. GWU IRB Policies

GWU IRB policies for the proper conduct of human research are provided within this Manual as well as in separate subject specific policies, e.g., Continuing Review Policy, Humanitarian Use Devices Policy, etc. Such subject specific research policies can be found at http://www.gwumc.edu/research/policies.htm. In addition, rules regarding the proper utilization of investigational drugs and devices can be found in the document entitled “GWUMC Standard Practice for Control and Use of Investigational Drugs and Devices in the University Medical Center” and other policies and procedures regarding the use of investigational drugs outside of the GWU Hospital setting.

II. What Constitutes Human Subject Research at GWU

Both federal regulations and GWU IRB policies define human subject research. The Common Rule defines a human subject as a living individual about whom an investigator conducting research (defined below) obtains data through intervention or interaction with the person or through individually identifiable private information. The FDA regulations define a human
subject as an individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A subject may be a healthy human/volunteer or a patient.

Moreover, federal regulations define research as a systematic investigation/study, including research development, testing, and evaluation, designed to develop or contribute to generalized knowledge. See 45 CFR 46.102(d). Examples of generalized knowledge include masters’ theses, doctorate dissertations, presentations, and journal articles. Pursuant to this definition, research also includes clinical trials, surveys/interviews, retrospective review of patient medical records, and experiments with blood/specimens. FDA considers research any use of a FDA regulated product except for use of a marketed product in the practice of medicine. Pursuant to FDA’s definition, the testing of a marketed product on a human subject (e.g., a marketed drug) for an intended use not yet approved for marketing constitutes research.

Pursuant to GWU policies, human subject research is defined as any activity involving human subjects, exploratory or hypothesis driven, which is designed to increase generalized knowledge. Such research typically involves human subjects, or any human tissue (living or dead), blood or any other bodily fluids, genetic material, ova, sperm, embryos, and/or certain record reviews, surveys, questionnaires, or interviews. Such research also includes drug and device studies, medical procedure studies, and research involving the review of clinical data sets.

As many people know, determining what constitutes human subject research is sometimes difficult, especially in the area of clinical case reporting and quality assurance/quality improvement (QA/QI). In an effort to assist researchers in determining whether their activities constitute human subject research, the GWU IRB drafted the following two guidelines, both of which can be accessed at [http://www.gwumc.edu/research/policies.htm](http://www.gwumc.edu/research/policies.htm)

Guidance on Medical Records Research vs. Case Reporting in the Clinical Setting; and
Guidance on Research vs. Quality Improvement/Quality Assurance

The following basic requirements must be met whenever human subject research is conducted at GWU (including GWU Hospital, and/or the MFA):

1. All human subject research must be reviewed and all non-exempt human subject research approved by the GWU peer review committee named the GWU Medical IRB prior to initiation of a study;

2. Written informed consent must be obtained from all potential human subjects prior to enrollment in any non-exempt research project unless waived or altered by the GWU Medical IRB in accordance with federal regulations;

3. Written research subject authorization must be obtained from all potential human subjects prior to enrollment in a research project involving the use or disclosure of PHI unless waived or altered by the GWU Medical IRB in accordance with federal regulations; and

4. All PIs and students must comply with research ethical standards, such as the principles covered in the Declaration of Helsinki.
(http://www.hhs.gov/ohrp/irb/irb_appendices.htm#j6) and the Belmont Report (http://www.hhs.gov/ohrp/humansubjects/guidance/belmont.htm). In addition, all PIs must certify their agreement to comply with such ethical standards by signing an investigator’s assurance agreement before engaging in human subject research. This agreement is available at http://www.gwumc.edu/research/forms.htm. Additionally, all students must certify their agreement to comply with such standards by signing a student research certification form, which is available at http://www.gwumc.edu/research/human/forms/nonmedical/Non-Medical%20Student%20Certification%20Documentation.doc.

You should ask the following questions when determining whether a proposed research project constitutes human subject research:

1. Is there an intervention or interaction with a living person that would not be occurring or would be occurring in some other fashion, but for this research? If you answer yes, the research constitutes human subject research and is subject to the policies and procedures outlined in this Manual. If, however, you answer no you still must ask the following question.

2. Will identifiable private data/information be obtained for this research in a form associable (e.g., the identity of the subject is or may be readily ascertained or associated with the information) with the individual? If you answer yes, the research constitutes human subject research. If, however, you answer no to this question and question (1) above, your research does not qualify as human subject research.

Even if your analysis brings you to the conclusion that your proposed research does not qualify as human subject research, you must nevertheless submit it to the GWU Medical IRB for review to ensure consistent regulatory compliance. Please note that the only individual at GWU with authority to determine whether a proposed medical study involving human subjects is exempt from IRB review is the GWU Medical IRB Chair or designee, with the concurrence of the Assistant Vice President or Health Research, Compliance, and Technology Transfer.

III. How Human Subject Research is administered at GWU

A. Jurisdiction of the GWU Medical IRB

The GWU Medical IRB, which is administratively supported by the Office of Human Research (OHR), is responsible for reviewing all human subject research and approving all non-exempt human subject research subject to its jurisdiction. As stated previously, the jurisdiction of the GWU Medical IRB is defined in its FWA commitment with HHS and by GWU IRB Policies. According to the FWA and GWU IRB policies, the jurisdiction of the GWU Medical IRB includes all human research (except research falling under one of the categories of research listed as exempt from IRB review under 45 CFR 46.101(b)) as follows:

- Research that is sponsored, e.g., supported or funded, either directly or indirectly, by GWU, GWU Hospital and/or MFA;
• Research conducted by or under the direction of any GWU, GWU Hospital, or MFA faculty or staff in connection with his/her institutional responsibilities. Please note that research conducted by or under the direction of a GWU, GWU Hospital, or MFA faculty or staff member in connection with personal consulting responsibilities falls outside the jurisdiction of the GWU Medical IRB;
• Research conducted by or under the direction of any GWU, GWU Hospital, or MFA faculty, staff, or student using any GWU, GWU Hospital, or MFA property or facility;
• Research conducted by students for academic credit regardless of where the research will be conducted. This category includes special projects, masters’ theses, doctoral dissertations; and/or
• Research involving the use of GWU, GWU Hospital, or MFA non-public information to identify or contact human research subjects or prospective subjects.

In other words, the GWU Medical IRB protects the rights and welfare of human subjects recruited to participate in research activities performed on GWU, GWU Hospital, or MFA premises and to any human research activities performed elsewhere by GWU, GWU Hospital, or MFA faculty, staff, or students. Please keep in mind that the responsibility of the GWU Medical IRB extends to research performed at “off campus” sites both within the United States as well as at foreign countries if GWU, GWU Hospital, or MFA faculty, staff, or students are PIs or listed as sub-investigators on the study.

B. Responsibilities of the GWU Medical IRB

Federal regulations/guidelines, the FWA, and GWU IRB policies govern GWU Medical IRB responsibilities, which extend to all research involving human subjects as described above. The GWU Medical IRB reviews applications involving human subject research and has the authority to approve, require modifications to, defer action on, or disapprove all such research conducted at or sponsored by GWU, GWU Hospital, or MFA faculty, staff, or students, including previously approved human subject research.

GWU Medical IRB responsibilities include:

• Reviewing all research projects involving human subjects prior to contacting potential human subjects or involving potential human subjects in proposed research;
• Ensuring that written informed consent is obtained from all potential human subjects prior to enrollment in a research study, unless waived or altered by the IRB in accordance with federal regulations;
• Ensuring that written research subject authorization is obtained from all potential human subjects prior to enrollment in a research study involving protected health information, unless waived or altered by the IRB in accordance with federal regulations;
• Providing prompt written notification to PIs, as well as other appropriate individuals, of IRB decisions on proposed research projects as well as requirements for modifications to previously approved research;
• Ensuring prompt reporting by PIs of planned changes in approved projects prior to making such changes except when proposed changes are necessary to eliminate apparent immediate hazards to research subjects;
Conducting continuing review. Please refer to the **GWU CHR IRB Medical and Non-Medical Continuing Review Policy** available at [http://www.gwumc.edu/research/policies.htm](http://www.gwumc.edu/research/policies.htm);

Ensuring that adequate additional protections are ensured for fetuses, pregnant women, prisoners, children, and mentally incapacitated individuals, as applicable. For more information regarding special classes of subjects, please refer to Chapter 5 of this Manual;

Suspending or terminating previously approved research when it is not conducted in accordance with IRB requirements or when research is associated with unexpected serious harm to subjects, and promptly reporting such reasons for suspension/termination to appropriate individuals/agencies. Please refer to the **GWU CHR IRB Reportable Events Policy** available at [http://www.gwumc.edu/research/policies.htm](http://www.gwumc.edu/research/policies.htm);

Placing restrictions on research projects, as appropriate;

Reviewing/monitoring emergency use of investigational FDA product. Please refer the **GWU CHR IRB Emergency Use of Investigational FDA Products Policy**, which will soon be available at [http://www.gwumc.edu/research/policies.htm](http://www.gwumc.edu/research/policies.htm);

Reviewing/monitoring use of Humanitarian Use Devices. For detailed information regarding this issue, please refer the **GWU CHR IRB Humanitarian Use Devices Policy**, which is available at [http://www.gwumc.edu/research/policies.htm](http://www.gwumc.edu/research/policies.htm);

Preparing and maintaining adequate documentation of the following IRB activities:

- Copies of all research protocols that have been reviewed, copies of all grant proposals or contracts for externally sponsored research, approved informed consent/assent/research subject authorization forms(s), continuing review reports, and any adverse events reports submitted to the GWU Medical IRB and/or GWU **Serious Adverse Event** (SAE) Subcommittee;
- Minutes of IRB meetings which demonstrate attendance at the meetings; actions taken by the IRB; vote on the actions taken including the number of IRB members voting for or against a particular IRB action as well as the number of IRB members who abstained (eligible to vote, but chose not to for any variety of reasons), or recused (ineligible to vote due to conflict of interest) themselves from voting; the basis for requiring changes in or disapproving research; and a summary of the discussion of controversial issues and their resolution;
- Records of continuing review activities;
- Copies of all correspondence (both formal and informal, e.g., email) between the IRB and the investigators;
- A list of IRB members as described in 45 CFR 46.103(b)(3);
- Written procedures for the IRB as described in 45 CFR 46.103(b)(4) and (b)(5); and
- Statements of significant new findings provided to subjects, as required by 45 CFR 46.116(b)(5).

**C. Composition of the GWU Medical IRB**

The GWU Medical IRB is currently made up of two committees, each consisting of approximately 10 – 15 members. The membership includes both full-time and part-time faculty, GWU general counsel, GWU research administrators, staff attorneys, nurses, pharmacists,
administrators, non-university-affiliated members, and laypersons. The GWU Medical IRB also includes both voting and non-voting (ex-officio) IRB members. A list of the current members of the GWU Medical IRB is on file with OHRP. This list is updated as needed. This current list is available on the OHR website at http://www.gwumc.edu/research/human/medical/roster.htm.

1. **Appointment of GWU Medical IRB Members**

The Provost & Vice-President for Health Affairs of the GWUMC (the Provost) appoints GWU Medical IRB members for a period of up to 1 year, corresponding with the fiscal year of the University, which runs from July 1st to June 30th. The process of appointment to the GWU Medical IRB is as follows: A recommendation for IRB appointment is made by the Chair of the GWU Medical IRB (the IRB Chair), or other University official in conjunction with IRB Chair, to the Associate and Assistant Vice-Presidents for the Office of Health Research, Compliance and Technology Transfer (AVPs). The AVPs approve or disapprove the candidate. Upon approval of the candidate by the AVPs, the candidate’s name is then forwarded to the Provost. If the Provost approves the candidate, an appointment letter is generated and mailed to the candidate. GWU Medical IRB members are not paid for their participation.

2. **Removal of GWU Medical IRB Members**

Each GWU Medical IRB member serves at the discretion of the AVPs, the Provost and IRB Chairs. Each GWU Medical IRB member is expected to attend at least 8 meetings per year. In the event that there are 4 or more unexcused absences in the course of the year, the AVPs and/or IRB Chairs may ask the member to step down.

3. **Selection and Appointment of the Chair of the GWU Medical IRB**

The AVPs appoints the IRB Chairs for a period of 5 years. This is a paid position. The IRB Chair may select up to two (2) Vice-Chairs to assist in the administration of IRB duties.

4. **Removal of Chair of the GWU Medical IRB**

The IRB Chairs serve at the discretion of the AVPs, with the concurrence of the Provost.

5. **Training and Education of GWU Medical IRB Members and IRB Chair**

The IRB Chairs are required to successfully complete the OHRP training entitled “Human Subject Assurance Training”, which is located at http://ohrp-ed.od.nih.gov. Successful completion of this course must occur prior to appointment. All other IRB members are strongly urged to take this training as well. In addition, the GWU Medical IRB Members and IRB Chairs must complete the following courses: “Computer-based training course for NIH IRB Members”, available at http://ohsr.od.nih.gov/irb_cbt/ and the “GWUMC HIPAA Training for Researchers” available at http://www.gwumc.edu/research/human/mohrforms.htm. Lastly, annual training seminars, along with on-going educational seminars, are held for all IRB members.
D. Operation of the GWU Medical IRB

1. Meeting Schedule

The GWU Medical IRB generally meets every second and fourth Tuesday of the month with the exception of the month of December. In December, the GWU Medical IRB meets on the second and third Tuesday of that month. There are times when the GWU IRB must change its meeting date in order to satisfy quorum requirements; however, this change in meeting date does not affect meeting submission deadlines. Deadlines for submission of protocols that need to be reviewed by the full committee are as follows:

- No later than close of business (COB) on the second Tuesday of the month for review at the fourth Tuesday IRB meeting;
- No later than COB on the fourth Tuesday of the month for protocols to be reviewed at the second Tuesday IRB meeting of the following month;
- For the third Tuesday IRB meeting in December, no later than COB on the first Tuesday of December.

Please note that these FCR deadlines only apply to IRB actions that require full committee review and approval. In other words, these FCR deadlines do not apply to studies/actions that can be processed under expedited review procedures, e.g., review and approval of studies that meet one of the expedited review categories. Any studies/actions that can be processed under expedited review procedures are reviewed on a first-come, first-serve basis.

2. Meeting Quorum

Any action taken at a full committee review (FCR) meeting can only occur with a quorum. Quorum is defined as the majority of the GWU Medical IRB voting members being present at a given IRB meeting. Also, please keep in mind that quorum must consist of at least one non-scientific IRB member; in other words, if there is no non-scientific member present, there is no quorum. Telephone participation satisfies the quorum requirement, but only when necessary and when the member participating via telephone has the same information the IRB members have at the meeting. Please note that mail (including email) reviews and votes are prohibited. Should the quorum fail during a given meeting (e.g., an IRB member needs to leave the meeting due to an emergency situation, on call, etc.), no further votes can be taken unless the quorum can be re-established.

3. Meeting Votes

Once it is determined that quorum has been satisfied, the meeting can proceed with IRB review of, and administrative action on, all research protocols action items listed on the agenda. In order for research to be approved, it must receive the approval of a majority of those members present at the meeting. See 45 CFR 46.108(b). For example, let’s assume 10 IRB members, out of a total of 15 members, are present at a particular meeting. In this
situation, quorum has been established to proceed with IRB actions; however, it is important to note that research reviewed at the meeting must receive the approval of at least 6 IRB members – a majority of the 10 IRB members present. Let’s assume that of the 10 members present; 5 vote for approval; 3 vote against approval; and 2 recuse themselves in accordance with the policy outlined below. In this situation, there is not a majority vote to approve the research as only 5 members voted for approval – less than a majority of those members present, e.g., 10. Please note that recusals convert into non-votes.

**IRB Recusal Policy** - Any GWU IRB member, voting or non-voting, who is involved in a study under consideration by the GWU IRB must remove (recuse) him/herself from the IRB discussions and/or actions relating to the study in which he/she is involved. Removal from IRB deliberations and actions will avoid any potential conflict of interest. Involved includes involved as a research team member, e.g., principal investigator, co-investigator, research coordinator or as a consultant on the study, e.g., medical specialist, biostatistician, etc.

4. **Meeting Format**

Most FCR IRB meetings follow the format of the finalized agenda, which is provided to all confirmed IRB attendees at least one week prior to the scheduled meeting. If requested, items/studies not listed on the finalized agenda may be discussed and voted on during a FCR meeting. Last minute add-on items/studies should only be voted on if IRB members have had sufficient time to review and consider the item/study.

Most FCR meetings are structured as follows:

- IRB members discuss any new items of interest (e.g., articles relating to human subject research, conflicts of interest, HIPAA, etc.). These items of interest are provided to IRB members either prior to the meeting or at the very beginning of the meeting.
- IRB members vote on the previous meeting minutes. The previous meeting minutes are generally forwarded to the IRB members via email prior to their attendance at the current meeting.
- IRB members review and discuss and vote on, if necessary, the finalized minutes from the most recent SAE Subcommittee meeting.
- IRB members review, discuss, and vote on any actions that have been taken on previously reviewed protocols, which received either a disapproval or deferral of action vote.
- IRB members review, discuss, and vote on continuing review protocols. Only one reviewer (primary) is assigned to conduct continuing review. For information regarding what information is provided to the primary reviewer, as well as the other IRB members, when reviewing a study for continuing review please refer to the **GWU CHR IRB Medical and Non-Medical Continuing Review Policy**, which can be accessed at [http://www.gwumc.edu/research/policies.htm](http://www.gwumc.edu/research/policies.htm).
• IRB members review, discuss, and vote on all new protocols. These protocols are reviewed under the primary/secondary reviewer system. Under such a reviewer system, a protocol is assigned to two reviewers, a primary reviewer and a secondary reviewer. Most often, the primary reviewer is a medical doctor whereas the secondary reviewer is not.

• IRB members review, discuss, and vote on major modifications to previously approved studies. As with continuing reviews, only one reviewer (primary) is assigned to review major modifications. For details regarding what information is provided to the primary reviewer, as well as other IRB members, please refer to Chapter 6 of this Manual.

• Lastly, the Chair/Associate Chair informs the committee of all IRB-related actions that have been acted upon on an expeditable/exempt basis. A summary of such studies and associated actions are included at the end of the meeting agenda. GWU Medical IRB members are free to provide comments and/or concerns regarding any such expeditable/exempt actions that have been taken.

IV. **IRB Actions**

The following is a list of actions available to the GWU Medical IRB following review of proposed human subject research studies, studies undergoing continuing review, and studies undergoing re-review due to proposed modifications to previously approved research. The GWU Medical IRB actions are communicated to the PI in writing usually within one week of the actions that have been taken.

**A. Final Approval**

The GWU IRB issues final approval memorandums whenever newly proposed studies, continuing review studies, or proposed modifications to already approved studies are IRB approved without any additional conditions needing to be satisfied. Such final approval memorandums inform PIs of the GWU IRB approval decision and that the study may begin (for newly proposed studies); may continue (for continuing review studies); or that the requested modifications may be implemented (for requests for modifications to already approved studies). In addition to receiving the approval memorandum, PIs receive any study related materials that require a stamp of GWU IRB approval, e.g., ICF, assent form, RSAF, recruitment materials, data-gathering instruments.

**B. Conditional Approval Pending Submission of Additional Information**

The GWU IRB issues conditional approval memorandums (for studies/actions requiring FCR) or conditional approval emails (for studies/actions qualifying for expedited review) whenever newly proposed studies, continuing review studies, or proposed modifications to already approved studies have been deemed approvable by the IRB, but only if the PI makes changes or provides additional information to the IRB. Such conditional approval memorandums/emails inform PIs of the changes/additional information requested. The memorandums/emails also inform PIs that they do not currently have IRB approval to begin a study (if newly proposed); to continue a study (if undergoing continuing review); or to implement modifications (if changes to a currently approved study are proposed).
C. Deferral of Action Pending Submission of Additional Information

The GWU IRB issues deferral of action memorandums (for studies/actions requiring FCR) whenever newly proposed studies, continuing review studies, or proposed modifications to already approved studies are not approvable by the IRB as currently presented to the full committee. Such deferral of action memorandums inform PIs of the following: (1) of the issues/concerns identified by the IRB; (2) that the full committee will reconsider the study once the PI addresses the issues/concerns raised by the IRB; and (3) that PIs do not currently have IRB approval to begin a study (if newly proposed); to continue a study (if undergoing continuing review) or to implement modifications (if changes to a currently approved study are proposed).

To date, the GWU IRB has not issued deferral of action memorandums for newly proposed studies, continuing review studies, or proposed modifications to currently approved studies that have been reviewed under expedited review procedures because all issues/concerns identified by the IRB Chair or designee have been, in most circumstances, communicated to the PI and addressed by the PI in an informal manner, i.e., via email correspondence; thereby obviating the need for a formal deferral of action memorandum. In the event that a PI refuses to address issues/concerns identified by the IRB Chair/designee, the PI will receive a deferral of action memorandum, which informs the PI that the study will be considered by the full IRB at it’s next meeting.

D. Disapproved

The GWU IRB issues disapproval memorandums (for studies/actions requiring FCR) whenever newly proposed studies, continuing review studies, or proposed modifications to already approved studies are disapproved by the IRB as currently presented to the full committee. Such disapproval memorandums inform PIs of the following: (1) the issues/concerns identified by the IRB; (2) an opportunity to request reconsideration; (3) the procedures that will occur if reconsideration is requested; and (4) that PIs do not currently have IRB approval to begin a study (if newly proposed); to continue a study (if undergoing continuing review); or to implement modifications (if changes to a currently approved study are proposed).

Pursuant to federal regulations governing expedited review procedures, an IRB Chair or designee may not disapprove a study/action reviewed via expedited review procedures; rather, an expedited review protocol may only be disapproved after being considered by the full committee. Thus, if a PI submits a study/action qualifying for expedited review and the IRB Chair or designee believes that it is not approvable, in lieu of generating a disapproval memorandum the IRB Chair or designee will inform the PI that the study/action will be considered by the full committee at the next IRB meeting.

The GWU IRB may disapprove a study/action for any of the following reasons: (a) the risks to subjects are too great in relation to benefit(s), if any; (b) there is an insufficient number of research staff to conduct the study; (c) research team members lack knowledge/education in human subject protection regulations; (d) PI or co-investigator is not qualified to conduct a study
requiring experience/expertise in a given medical specialty; and/or (e) moral/ethical considerations. *Please note that this is not an all-inclusive list.*

V. **Requirements for Responding to Comments Raised During the IRB Review Process**

PIs are asked to respond to IRB correspondence within one month of receipt of the correspondence, when feasible. The IRB believes that this amount of time is sufficient in most circumstances. Nevertheless, the IRB recognizes that some IRB memorandums/requests may require PIs to correspond with outside entities, e.g., sponsors, regulatory agencies, etc., which could prolong the response time. Given this possibility, please keep in mind that this 30-day response time is simply a guide. As a general rule, the IRB will take administrative action to withdraw or terminate a study at 30 days, unless the PI submits the requested information or requests an extension within the initial 30-day response time or the IRB determines that it is in the best interest of subjects to keep the study active. When such a request or IRB determination is made, the IRB will extend the initial 30-day response time for one or more additional 30 days; after which the IRB will take administratively withdraw or terminate a study for failure to respond to IRB issues.

VI. **Effect of IRB Actions**

Even though a research project may receive IRB approval, the research may be subject to further review from GWUMC institutional officials. Such GWUMC institutional officials may subsequently disapprove, suspend, or terminate a project for any variety of reasons, including research not meeting the policies/goals/obligations of the PI’s department. However, please note that a GWUMC institutional official **MAY NOT** overrule the GWU Medical IRB and approve a study that was not approved by the IRB.
CHAPTER 2: COOPERATIVE RESEARCH ENDEAVORS

I. Types of Cooperative Research Endeavors

It is anticipated that there will be an increase in the number of human subject research protocols involving both GWU, GWU Hospital, and/or MFA faculty, staff, or students and non-GWU investigators/institutions/organizations. This type of research is known as cooperative research. Such cooperative research endeavors are often mutually beneficial to GWU and the non-GWU investigator/institution/organization. Moreover, such cooperative research can be beneficial to the subjects themselves, e.g., offering a subject a follow-up site that is closer to his/her home than GWU.

Under cooperative research endeavors, one or more institutions are responsible for safeguarding the rights and welfare of human subjects. With the approval of OHRCTT, GWU, GWU Hospital, or MFA faculty, staff, or students may elect to participate in a cooperative project whereby GWU enters into a joint review arrangement, relies upon the review of another qualified IRB or makes similar arrangements for avoiding duplicative review, approval and oversight. When no such cooperative research agreements exist, the GWU Medical IRB will review, approve, and provide oversight according to this Manual.

Historically, OHRP has approved three basic types of assurances: Federalwide Assurance (FWA), Cooperative Project Assurance (CPA) and Single Project Assurance (SPA). In December 2000, OHRP developed an IRB Registration and a new Federalwide Assurance Process intended to: 1) create a new registry of IRBs; and 2) streamline the assurance process to significantly reduce the administrative burden on individual institutions, other federal departments and agencies and OHRP. Under the new system, each legally separate entity that engages in federally supported human subject research will need its own Assurance.

For more information regarding the currently available types of cooperative research endeavors under the new OHRP Assurance System, please contact OHRCTT, 712 Ross Hall.

II. Considerations Taken Into Account When Reviewing Cooperative Research Endeavors

The GWU Medical IRB must review each cooperative research endeavor on a case-by-case basis. The following is a list of items the GWU Medical IRB will consider when deciding whether to engage in cooperative research endeavors:

- The professional competence of non-GWU investigators and/or the standards of non-GWU institutions/organizations: the GWU IRB will conduct a professional competency and an institution/organization standards evaluation to determine whether the competency of non-GWU investigators and standards of non-GWU institutions/organizations are satisfactory.
• The amount of responsibility placed upon GWU, GWU Hospital, or MFA faculty, staff or students in the conduct of the research: the greater the responsibility placed upon GWU individuals the simpler it will be for the GWU Medical IRB to review and approve the research. Where primary responsibility involves a non-GWU investigator/institution/organization, the IRB will examine the need for the primary role to be taken on by a non-GWU investigator and the benefits of that role for the subjects and the research.

• The degree of risk the subjects will be exposed to under the cooperative research endeavor: prior to GWU Medical IRB approval, the IRB will need to know whether there are adequate facilities and/or expert care for the subjects in the event of study problems. Such considerations/questions can only be answered through an analysis of each protocol and the roles of the various personnel and facilities. The protocol must include sufficient information for this analysis.

• That appropriate legal documents are drafted given that GWU may be exposed to liability for research endeavors that involve non-GWU affiliated investigators/institutions/organizations. The GWU Medical IRB will solicit GWU General Counsel advice whenever outside cooperative research is proposed.

Whenever research will be conducted on GWU, GWU Hospital, or MFA patients/subjects by non-GWU investigators the following requirements must be satisfied:

• A GWU, GWU Hospital, or MFA faculty or staff member must be listed as the PI or sponsor;
• The GWU Medical IRB must approve the study; and
• The study must be approved by the IRB of the non-GWU institution, if there is one. If not, the non-GWU institution will have to enter into an appropriate cooperative research agreement with GWU establishing the GWU Medical IRB as the IRB of record for the study. If such a situation arises where an appropriate cooperative research agreement will need to be entered into, please contact OHR; and
• All other human subject research requirements (e.g., investigator agreement, education, copy of current medical record, etc.) are followed.

III. Considerations Taken Into Account When GWU is Grantee or Prime Awardee

According to OHRP guidance, whenever an institution “wins” a direct HHS award to support human subject research it is considered the awardee institution and, as such, bears ultimate responsibility for protecting human subjects under the award. However, this ultimate responsibility, which lies with the IRB affiliated with the awardee institution, varies depending on the type of activities that are being conducted at the awardee site. The most common types of activities (and corresponding IRB levels of responsibility/review) that have been conducted at GWU, as the awardee institution, have included the following:

A. GWU Employees Maintaining Statistical Centers for Multi-Site Research

With this type of activity, i.e., obtaining, receiving, or possessing private information that is individually identifiable (either directly or indirectly through coding systems) for the purpose of
maintaining a “statistical center,” there is no interaction or intervention with subjects; as a result the principal risk associated with such activities is potential harm resulting from breach of confidentiality. The GWU Medical IRB has determined that the only way it can ensure that this potential breach of confidentiality risk is minimized is by reviewing and approving the model collaborative protocol and informed consent/assent/research subject authorization form(s) associated with such studies prior to forwarding the protocol and informed consent/assent/research subject authorization form(s) to the participating clinical sites for local site IRB review and approval. In addition, the GWU Medical IRB must be able to find and document that the statistical center has sufficient mechanisms in place to ensure the following:

- The privacy of subjects and the confidentiality of data are adequately maintained, given the sensitivity of the data involved;
- Each collaborating institution holds an applicable OHRP-approved Assurance;
- Each protocol is reviewed and approved by the IRB at the collaborating institution prior to enrollment of subjects;
- Informed consent is obtained from each subject in compliance with HHS regulations; and
- Research subject authorization is obtained from each subject enrolled in a study involving protected health information.

B. GWU Employees Maintaining Coordinating Centers for Multi-Site Research

The GWU Medical IRB has concluded that whenever GWU faculty, staff, or students maintain an operations/coordinating center for a multi-site collaborative research project, the GWU Medical IRB must review and approve the model collaborative protocol and informed consent/assent/research subject authorization form(s) associated with such projects prior to forwarding the protocol and informed consent/assent/research subject authorization form(s) to the participating clinical sites for local site IRB review and approval. In addition, the GWU Medical IRB must find and document that the operations or coordinating center has sufficient mechanisms in place to ensure the following:

- That management, data analysis, and data safety and monitoring systems are adequate, given the nature of the research involved;
- Sample protocols and informed consent documents are developed and distributed to each collaborating institution;
- Each collaborating institution holds an applicable OHRP-approved Assurance;
- Each protocol is reviewed and approved by the IRB at the collaborating institution prior to enrollment of subjects;
- Any substantive modifications by the collaborating institution of sample consent information related to risks or alternative procedures is appropriately justified;
- Informed consent is obtained from each subject in compliance with HHS regulations; and
- Research subject authorization is obtained from each subject enrolled in a study involving protected health information.

For additional guidance regarding ways in which an institution can engage in research, and thus become responsible for human subject protection, please refer to OHRP’s January 26, 1999
CHAPTER 3: GENERAL IRB SUBMISSION REQUIREMENTS

This chapter provides information regarding what constitutes a complete IRB submission package for GWU IRB review. What follows is a list of items that must be submitted to the IRB in order for an IRB Submission package to be considered complete. Please note that the number of copies of each item differs depending on the type of review requested.

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<th>Items of Information</th>
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<td>Protocol Summary</td>
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<td>Data Gathering Instruments (surveys, questionnaires, etc)</td>
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<td>Grant Application or Contract (for externally-funded studies)</td>
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<td>CVs/Resumes of PI and sub-investigators &amp; faculty sponsors for student research projects, unless previously submitted</td>
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<td>Partial Waiver of RSAF for Recruitment Purposes for studies involving PHI (may require signature of CE’s Privacy Off)</td>
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Some of the documents outlined above are described in detail below. The GWU Medical IRB hopes that this detail will provide insight into what circumstances necessitate the submission of certain information and why such information is required.

I. Medical IRB Submission Form – ALL Studies

The Medical IRB Submission Form is available online and can be downloaded from [http://www.gwumc.edu/research/forms.htm](http://www.gwumc.edu/research/forms.htm). The form includes all relevant information that must be considered by the GWU Medical IRB when conducting IRB review of human subject research. Below, you will find sections of the Medical IRB Submission Form that are being clarified as a result of requests from research community members, a recent change in policy, or the implementation of a new policy. Sections of the Medical IRB Submission Form that do not require clarification or have not been recently modified or recently implemented are not outlined below.

A. Type of IRB Review Requested

PIs have always been asked to identify the type of IRB review s/he believed was appropriate for his/her study, e.g., full committee review (FCR), expedited review (ER), or exempt from IRB review (EX). However, this identification step simply entailed checking off the type of review he/she thought was most appropriate for his/her study. Previously, if PIs requested ER or EX, they were not required to identify which expedited or exempt category his/her study fell under. Now, PIs must identify both the type of IRB review s/he believes is appropriate for his/her study as well as complete either the NEW Expedited Review Request Form or the NEW Exempt from IRB Review Request Form, as applicable. With these new forms, the PI is asked to specifically identify which of the expedited or exempt categories s/he believes his/her study falls. Both of these forms are available online at [http://www.gwumc.edu/research/forms.htm](http://www.gwumc.edu/research/forms.htm).

Under this change in procedure, PIs have to do the following:

1. **FCR Studies.** Check off FCR on the Medical IRB Submission Form and complete the form in its entirety.
2. **ER Studies.** Check off ER on the IRB Submission Form, complete the form in its entirety, and complete the Expedited Review Request Form.
3. **EX Studies.** Check off EX on the IRB Submission Form, complete the form in its entirety, and submit the Exempt from IRB Review Request Form. **Please note that studies qualifying as exempt from IRB review are NOT required to adhere to federal regulations governing the protection of human subjects (i.e., 45 CRR Part 46), including the requirement to obtain informed consent. As a result, any PI asking for exempt from IRB review need not submit an informed consent form or a waiver/alteration of informed consent request form because such studies are automatically exempt from informed consent regulatory requirements.**

B. Type of Informed Consent/Assent Requested

1. **Informed Consent**
With the new Medical IRB Submission Form, PIs are queried on the type of informed consent being requested, i.e., complete informed consent, waiver of written documentation of informed consent, waiver of or alteration to the informed consent process, or waiver of informed consent in emergency research.

Pursuant to the Common Rule, under certain circumstances a PI may request one of two kinds of waiver of or alteration to the usual requirement to obtain written informed consent from human subjects. The first is a waiver of written documentation that informed consent was obtained. The second is a waiver of or alteration to the actual requirement to obtain informed consent. Pursuant to those same regulations, an IRB can approve a waiver of or alteration to the informed consent process when it finds and documents that a particular study meets the waiver or alteration criteria. The operative word in the previous sentence is *finds*.

Under the old IRB submission process, even if a PI believed that his/her proposed study met the criteria for waiver of or alteration to informed consent he/she was not required to provide justification as to why s/he believed the study met the waiver or alteration criteria. Given that there was no uniform way for PIs to document on the IRB Submission Form or in supporting documentation that his/her study met the applicable criteria, it was often difficult for the GWU Medical IRB to make such a finding without first contacting the PI to discuss the study. Many times, this additional step led to delays in a PI receiving IRB approval. As a result, PIs must now check off on the IRB Submission Form one of four new options, depending on what the PI is requesting in reference to informed consent.

In addition to this new informed consent section, all PIs requesting a waiver of written documentation of informed consent or a waiver of or alteration to the entire informed consent process must submit a NEW Waiver or Alteration to Informed Consent Request Form along with the IRB Submission Form. This NEW Waiver or Alteration Form is available at [http://www.gwumc.edu/research/forms.htm](http://www.gwumc.edu/research/forms.htm).

The Waiver of or Alteration of Informed Consent Request Form will assist the PI in determining whether his/her study qualifies for one of the waiver/alteration options as well as assist the GWU Medical IRB in making a waiver/alteration finding. **Part I of the Form should be completed when a PI requests waiver of written documentation of informed consent (i.e., the PI will obtain verbal informed consent in lieu of written informed consent). Part II of the Form should be completed when a PI requests waiver of the informed consent process in its entirety or requests a waiver of certain elements of informed consent.**

For more information on these various informed consent options, as well as the waiver of informed consent option in emergency research protocols designed to evaluate emergency care interventions, please refer to Chapter 4 of this Manual.

2. **Assent**

For studies involving children, the PI is now asked to indicate the type of assent being requested. The assent options are either none if the children proposed to be involved in
the study are not capable of providing assent or a study specific assent form for those studies in which children are capable of providing assent. For more information regarding obtaining informed consent/assent for studies involving children please refer to Chapter 4 of this Manual.

C. Type of Information Being Used or Disclosed as Part of a Study

As a result of the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule research-related provisions, the GWU IRB has introduced a new section into the Medical IRB Submission Form. As you may know by now, the type of data proposed to be used or disclosed in a study determine whether the research-related provisions of HIPAA will apply to a given study. Thus, PIs are now asked to indicate the type(s) of data being used or disclosed as part of a proposed study. PIs have been provided with the HIPAA Worksheet for Determining the Type of Research Data Being Used or Disclosed for guidance in assisting them in determining the type of research data to be used/disclosed. The worksheet is available at http://www.gwumc.edu/research/forms.htm

Under this new section, PIs are now asked to check one or more of the following boxes, as applicable for each study:

- No health information will be used or disclosed in this study.
- No protected health information will be used or disclosed in this study.
- De-identified information will be used or disclosed in this study.
- Limited data set information will be used or disclosed in this study.
- Protected health information will be used or disclosed in this study.

If a PI checks that he/she is proposing to use or disclose either Limited Data Set Information (LDS) or Protected Health Information (PHI) in his/her study, the PI must also complete a section of the Medical IRB Submission Form entitled Type of Research Subject Authorization Requested. The new section directs the PI to check the type of research subject authorization option he/she proposes to use for the study. The options include: a complete research subject authorization form; a waiver of or alteration to the research subject authorization; or for studies involving limited data set information, a data use agreement option. For more information on each of these options, please refer to Chapter 9 of this Manual.

D. Investigator Team Information

Only GWU faculty and/or staff, including residents and fellows, can be named as a PI for human subject research studies. If a non-GWU faculty member or staff is listed as the PI for a study, the IRB Submission Package will be returned to the PI for modification. Moreover, if a student researcher wishes to conduct a study, the student’s faculty advisor must be designated as the PI on the project; the student researcher may be designated as the sub-investigator and/or the research coordinator.

In order to assist the GWU Medical IRB in identifying the appropriate category for each PI, the PI is asked to indicate his/her appropriate category as either GWU faculty, GWU fellow, GWU staff, GWU resident, or other.
E. CVs/Resumes

As part of the IRB submission process, each PI, sub-investigator (if any), and person involved in the informed consent process (if different from PI or sub-investigator(s)) is now required to submit his/her CV or resume if his/her CV/resume has not been previously submitted to the GWU IRB. The GWU IRB reviews the CVs to assess the qualifications of the research team members. The PI’s (and sub-investigator(s), if any) professional development must be considered in relation to the complexity of the proposed protocol and the resulting degree of risk to human subjects. This is why the GWU IRB requests the CVs of the PI and sub-investigators, if any, as part of the IRB submission process. As a consequence of this review, the GWU Medical IRB may require less experienced researchers to be sponsored by more experienced researchers. Protocols that require skills beyond those held by the PI will be modified to meet the investigator's skills or have additional qualified personnel added. If the IRB determines that no PI is qualified for a particularly complex study, the study will be disapproved. For instance, the GWU Medical IRB may request a researcher with relevant experience in the disease, condition, or medical specialty being studied to be the PI; and a researcher without such, or less, experience be listed as a sub-investigator. Moreover, the GWU Medical IRB reviews the CVs of the individual(s) leading the consent process in order to assess the individual(s)’ knowledge in the disease/condition being studied, the individual’s affiliation with GWU, if any, and the extent of knowledge of the individual regarding the informed consent process specifically and human subject protection regulations generally.

Please note that only GWU affiliated faculty, staff, or students may consent GWU subjects into human subject research studies.

F. Letters of Assurance

All PIs must have on file with the GWU IRB a signed Investigator’s Assurance Agreement. The agreement is submitted only once; the agreement governs all future human subject studies. The agreement is available at http://www.gwumc.edu/research/forms.htm. The agreement certifies that the PI has read the GWU Assurance, understands the requirements for involving human subjects in research, and agrees to abide by the requirements.

Moreover, all student researchers must have on file with OHR a signed Human Subjects Research Agreement. As with the Investigator’s Assurance Agreement, the student researcher agreement must be submitted only once; the agreement will govern all future human subject studies. This agreement can be found at http://www.gwumc.edu/research/human/forms/nonmedical/NonMedical%20Student%20Certification%20Documentation.doc.

In order to find out whether you have such agreements on file with OHR, please call 202-994-2715.

G. Education
1. **HIPAA Training.**

   All faculty, staff and students associated with the GWUMC who plan to submit a study to the GWU Medical IRB must successfully complete the HIPAA Training for GWU Researchers and Research Administrators, which can be located at [http://www.gwumc.edu/research/forms.htm](http://www.gwumc.edu/research/forms.htm) prior to submitting a study to the GWU Medical IRB for review. All faculty, staff and students NOT associated with the Medical Center, but who plan to submit a study to the GWU Medical IRB should follow the HIPAA training policy for non-medical researchers, available at [http://www.gwumc.edu/research/human/forms/hipaa/HIPAATrainingNonMedicalOrUniversityBasedDepartments_Approved71003.doc](http://www.gwumc.edu/research/human/forms/hipaa/HIPAATrainingNonMedicalOrUniversityBasedDepartments_Approved71003.doc), unless otherwise directed by the GWU IRB.

2. **NIH Sponsored Research Training.**

   Effective October 1, 2000, NIH requires all key staff members (principal investigators, co-investigators, and other staff) involved in any project, funded in whole or in part by NIH, to undertake a required education course on the protection of human subjects in research. The NIH Training program can be found at [www.gwumc.edu/research/disclaimer.htm](http://www.gwumc.edu/research/disclaimer.htm). This site is aimed at PIs conducting research in the medical or physical sciences. Please note that while the training program refers to the NIH Federalwide Assurances (FWA), you are expected to conduct any work initiated at GWU, GWU Hospital, and/or the MFA under the GWU FWA. Once you have completed this program, you MUST send your results to OHRCTT. Further information regarding this policy can be located at the following address: [http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html](http://grants.nih.gov/grants/guide/notice-files/NOT-OD-00-039.html).

### H. Department Chair/Dean Signature

This is the section where the department chair or school dean signs the Medical IRB Submission Form. The signature of the chair/dean ensures that s/he has reviewed the research proposed to be conducted by his/her faculty, staff, and/or students and has approved the research. In addition, the department chair/dean is the individual responsible for local oversight of the study.

Be advised that whenever a department chair or school dean is listed as the PI for a given study, his/her signature is not acceptable due to the appearance of a conflict of interest. Alternatively, in such circumstances the supervisor of the department chair or school dean must sign the IRB Submission Form. Unsigned or inappropriately signed IRB Submission Forms will be returned to the PI and/or his/her research team for modification.

### I. Project Information

Whenever GWU is named the prime awardee institution on a multi-center research project or a GWU, GWU Hospital, or MFA faculty, staff, or student is named the principal investigator of an entire multi-center study, the named GWU PI must complete the **Multi-center Project Information Supplemental Form** of the Medical IRB Submission Form and include IRB approval documentation from the non-GWU institutions or organizations involved. The documentation from non-GWU institutions/organization that must be submitted as part of the
GWU Medical IRB submission package is outlined in the Multi-Center Project Information Supplemental Form.

J. Sponsor Information

All externally sponsored studies must undergo Office of Research Services (ORS) review at the same time the protocol is undergoing IRB review. As a general matter, ORS will not sign off on a final research contract until the research protocol has received IRB approval. However, there is one exception to this general rule, which involves research contracts/applications/proposals that lack definitive plans for the involvement of human subjects.

Some applications for federal grants, cooperative agreements, or contracts require the submission of applications/proposals at a time when definitive plans for the involvement of human subjects have not yet been finalized and set forth in the application proposal, e.g., only preliminary plans have been developed regarding whether human subjects will be involved in the research related to the applications/proposals. These types of applications/proposals include institutional type grants where selection of specific projects is the institution’s responsibility; research training grants in which the activities involving human subjects has not yet been selected; and projects in which human subjects’ involvement will depend upon completion of instrument, prior animal studies, or purification of compounds.

Such contracts/applications/proposals which lack definitive plans for the involvement of human subjects will not be reviewed and approved by the GWU IRB at this preliminary juncture because there are no human subject issues to be addressed. However, once definitive plans for the involvement of human subjects are finalized and set forth in the proposed protocol, the GWU Medical IRB will review the study. GWU IRB review of studies at this time ensures that no human subjects will be involved in any research protocol until the protocol has been reviewed and approved by the GWU IRB. Please refer to 45 CFR 46.118 for further guidance.

K. Protocol Information

The protocol information section of the new IRB Submission Form queries PIs about the following:

- What aspects of the study are retrospective in nature and what aspects of the study are prospective in nature?
- Whether the data involved in the study will be identifiable when the PI gains access to the data (i.e., looks at the data);
- The source of certain research data;
- Whether the proposed study involves genetic research. If the proposed study involves recombinant genetic research, which is research indicated vs. medically indicated, the PI is directed to obtain approval by the GWU Institutional Recombinant DNA Committee before submitting the protocol to the GWU IRB for review and approval; and
- Whether the proposed study will involve the use of radiation and/or lasers and where such use will occur, i.e., at GWU Hospital/MFA or at GWU. If a proposed research study includes the use of radioisotopes, X-rays, etc., the PI must indicate the appropriate
radiation use associated with the study (e.g., medically indicated or research indicated). If the radiation use is research indicated, the PI must obtain approval of the study by the applicable committee/individual prior to submitting the proposed research to the GWU Medical IRB for review.

L. Human Subject Participant Information

The human subject participant information section of the new IRB Submission Form queries PIs about the following:

- The populations proposed to be studied;
- Justification for excluding certain populations;
- Whether the proposed research involves the PHI of decedents; and
- Identification of any vulnerable populations proposed to be studied, if any.

In addition, this section of the IRB Submission form includes instructions on what is required if a study involves the participation of subjects who are not proficient in English.

M. Subject Recruitment

The rights to privacy and confidentiality of potential human subjects, as well as the voluntary nature of participation in human subject research, must override any investigators efforts to identify and recruit potential subjects. With this underlying premise in mind, the GWU Medical IRB has modified the subject recruitment section of the Medical IRB Submission Form to include a more detailed inquiry into proposed recruitment practices. This more detailed inquiry will assist the GWU Medical IRB in determining whether proposed recruitment practices run counter to the recruitment premise stated above. When completing this section of the Medical IRB Submission Form, please keep in mind the following GWU Medical IRB guidance regarding Acceptable Recruitment Practices. The recruitment practices listed below are acceptable only when the investigator obtains prior IRB approval of the recruitment practices.

The GWU IRB has deemed the following recruitment practices acceptable under the Common Rule only, i.e., the recruitment practices do not involve the use or disclosure of PHI. Please see Chapter 9 of this Manual for additional guidance regarding recruitment practices involving the use or disclosure of PHI. In short, recruitment practices involving PHI will need to fall within one of the acceptable recruitment practices listed below as well as meet any additional HIPAA requirements.

1. The Use of Publicly Placed Flyers, Posters, Brochures, and Advertisements on Websites and/or in Newspapers and Other Such Publications.

Such recruitment materials, whether placed in GWU facilities or in non-GWU facilities, are considered to be an acceptable recruitment practice because the recruitment materials avoid any possibility of coercion and promote voluntary participation. Such publicly placed recruitment materials should only include the following information:
• The name of the investigator and contact information, including the name of GWU;
• A simple and concise description of the purpose of the research;
• General eligibility criteria for participation;
• A truthful description of the possible benefits, which may result from participation in the research. If there are no benefits, please indicate whether subjects are paid for their participation or receive free treatment; and
• For studies recruiting minors, the recruitment material should explicitly state that parental consent is required for participation.

Remember, such recruitment materials must be reviewed and approved by GWU IRB prior to use. Hard copy recruitment materials that are not professionally produced must contain a GWU IRB stamp of approval (e.g., GWU produced flyers, posters, etc.). Recruitment materials that are to be added to a website must contain a statement that the GWU IRB has reviewed and approved this recruitment advertisement.

2. A Treating Non-Covered Health Care Provider (HCP) who is to be involved in a study, either as a PI or a member of the research team, speaks to his/her patients about the option of enrolling in his/her study.

When a HCP wishes to recruit his/her patients into a study in which he/she is involved, the HCP can simply discuss the study with his/her patients at the patient’s next scheduled visit or provide his/her patients with a GWU IRB approved invitational, informational letter regarding the proposed research at the patient’s next visit. Alternatively, if the HCP wishes to recruit subjects prior to the patient’s next scheduled visit or for patients that do not have a visit scheduled, the HCP may mail a GWU IRB approved invitational, informational letter regarding the proposed research to patients/potential subjects for review and consideration. Follow-up contact with individuals who fail to respond to the invitational/introductory letter should not occur.

3. A Treating Non-Covered HCP, not involved in a study, uses his/her own knowledge of a colleague’s study and his/her knowledge of his/her patient’s condition to inform his/her patients about the colleague’s study.

In this situation, the treating HCP should be the individual that introduces the study to his/her patients. The treating HCP can introduce the study by discussing the study with his/her patients at the patient’s next scheduled visit or providing his/her patients with a GWU IRB approved invitational, informational letter regarding the proposed research at the patient’s next visit. If the letter option is chosen, the letter should come from the treating HCP and can be signed by the treating HCP as well as the PI of the study. The invitational/introductory letter should explain the following:

• There is a research study being conducted;
• Who is conducting it;
• What is the purpose of the study; and
• Why the particular individual is being asked to participate (e.g., studying his/her medical diagnosis).

At this point, two possibilities exist. First, the HCP may give the PI’s contact information to the patient and the patient contacts the researcher. Alternatively, the HCP may give the patient’s contact information to the PI, with the approval of the patient, and the PI initiates the contact. Under this scenario, the HCP should only give the researcher the names of those individuals who showed an interest in the study. The researcher should not be provided with the names of individuals who did not show an interest in the study.

Again, such invitational/informational letters must be reviewed and approved by the GWU Medical IRB prior to implementation.

N. Subject Compensation

The GWU Medical IRB does not discourage subject compensation; however it does discourage compensation that constitutes or could constitute undue inducement to participate in a study (e.g., the compensation alone serves as the main, if not only, reason why a human subject volunteers). Thus, the GWU Medical IRB considers reimbursement for inconvenience or other costs to subjects resulting from participation in a given study to be acceptable forms of compensation. Such acceptable costs include fees associated with private transportation (e.g., parking fees) or public transportation (e.g., metro or taxi fees), lost time from work, etc. Please note that if subject compensation is proposed, such compensation should be prorated to ensure that subjects are compensated for only those phases of the trial they have completed. For instance, a PI should not provide compensation in full at the time the subject enrolls in a study. Alternatively, the PI of a long-term study should not hold back compensation until all phases of the long-term study have been completed. To do so could be seen as coercive; subjects may feel compelled to complete the study in order to receive compensation; whereas subjects may have withdrawn from the study had compensation being provided on a prorated basis.

The GWU Medical IRB will review both the amount and method of disbursement (e.g., cash, check, metro fare cards) to ensure that the remuneration does not constitute undue inducement. If the GWU Medical IRB approves a study that allows for subject compensation, the informed consent must disclose such compensation.

O. Finders Fee

Finder’s fees to healthcare providers or others are unacceptable to the GWU Medical IRB unless the fee is provided to individuals who are tasked with duties beyond simply referring subjects. Such additional duties can include conducting eligibility screening, giving questionnaires/surveys/interviews, providing expert advice on the protocol, etc. Such nominal compensation cannot be contingent upon a subject being enrolled in a study, the agreement of a subject to participate in the study, or completion of the protocol. If the GWU Medical IRB approves a study that allows for nominal compensation to referring healthcare providers or others, the informed consent must disclose such compensation.
P. Confidentiality and Privacy for Subjects

In response to HIPAA, the GWU IRB is asking more detailed questions regarding the type of data to be used or disclosed during a study, the identities of the individuals that will have access to the PHI, how the data will be kept during the study, and how the data will appear when the PI/research team obtains and stores the data.

Q. IND/IDE/510(k) Information

This section has been added to clarify when an IND/IDE/510(k) is required for a clinical trial and that the GWU IRB obtains a copy of the IND/IDE/510(k) Food and Drug Administration (FDA) notification memorandum when one is required. For further guidance regarding when an IND/IDE is required for a clinical trial, please refer to the George Washington University Committee on Human Research Institutional Review Board Guidance Regarding IND and IDE Applications - When are they Required for a Clinical Research Study, which can be found at http://www.gwumc.edu/research/policies.htm

R. Conflicts of Interest Information

Every PI must complete this section; failure to complete this section will result in the IRB Submission package being returned to the PI. For guidance regarding a potential conflict of interest that should be reported, please refer to the GWU Policy on Conflicts of Interest and Commitment, which can be found at http://www.gwu.edu/~research/COhtm. For FDA’s guidance on Financial Disclosure by Clinical Investigators, please go to www.fda.gov/guidance/financialdis.html. For guidelines interpreting the application of the PHS regulations to research conducted or supported by NIH that involve human subjects go to http://grants1.nih.gov/grants/guide/notice-files/NOT-OD-00-040.html.

If a PI discloses on the IRB Submission Form that s/he has a reportable conflict of interest, the PI must obtain approval of the study from the GWU Conflicts of Interest (COI) institutional official, which may involve the Conflicts of Interest (COI) Committee, prior to submitting his/her proposed research to the GWU Medical IRB for review. If the COI Committee finds that a PI has a reportable interest in a particular study the PI will be notified of this finding. Along with the notification, the PI will be provided with a list of options, if appropriate, that the COI Committee has identified as acceptable ways to manage the interest. Such options can vary from removal of the PI from the study in its entirety to prohibiting a PI from engaging in particular aspects of the study, e.g., consenting potential subjects.

As with finders’ fees, if the GWU Medical IRB approves a study that includes a conflict of interest the informed consent must disclose the conflict of interest and explain how the conflict was or will be managed.

II. Protocol – ALL Studies
A **protocol** is the formal design or plan of a research study/activity. The protocol includes, among other things, a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data. In other words, a protocol is the work plan for the research. A protocol is required for all studies. For specific information regarding what must be included in all medical research protocols, please refer to the GWUMC Guideline for Writing Research Protocols Document, which can be accessed at [http://www.gwumc.edu/research/human/forms/medical/Outline%20for%20Writing%20Research%20Protocols.doc](http://www.gwumc.edu/research/human/forms/medical/Outline%20for%20Writing%20Research%20Protocols.doc).

PIs involved in drug/device/biologic/procedure studies must pay special attention to the Risks and Benefits Section of the protocol. For all drug/biologics trials, the risk and benefits section should be based on an adequate and comprehensive literature search of the safety of the drug or biologics under study. At the conclusion of this literature search, the PI must be able to conclude that the study drug/biologic is sufficiently safe for use in the subjects of the study. For more information please refer to the Johns Hopkins University Guideline for Determining an Adequate and Comprehensive Literature Search at [http://irb.jhmi.edu/Guidelines/LiteratureSearch.doc](http://irb.jhmi.edu/Guidelines/LiteratureSearch.doc).

Please note that under the Financial Considerations Section of the protocol PIs must describe who will be responsible for the costs associated with the study, e.g., who is responsible for routine medical care rendered under the protocol vs. who is responsible for research related care rendered under the protocol. The PI must itemize all costs the subject will be responsible for and all costs the sponsor will be responsible for. As a general rule, all standard of care/routine medical care costs may be borne by the subject. All non-routine/research related care should be borne by the sponsor of the study.

### III. Protocol Summary – All Studies

The protocol summary is an abstract of the full research protocol. The protocol summary should be 1-2 pages in length and should cover the following items:

- Summary;
- Purpose;
- Research plan including description of experimental/placebo groups and study design;
- Study objective;
- Study population;
- Risks and side effects;
- Endpoints of research; and
- Statistical explanation for the number of subjects to be enrolled.

### IV. Forms FDA 1571 and 1572 – All Applicable Drug Studies

As part of the GWU IRB review process, the GWU Medical IRB requires submission of signed completed FDA forms1571 and/or 1572, as applicable. A Form FDA 1571 is required to be submitted as part of the GWU IRB submission package when a GWU principal investigator is considered the sponsor-investigator of an IND study. A sponsor-investigator is defined as
individual who both initiates and conducts an investigation and under whose immediate direction
the investigational drug is administered or dispenses. The requirements applicable to a sponsor-
investigator include both those applicable to an investigator and a sponsor. Alternatively, a Form
FDA 1572 is required to be submitted as part of the GWU IRB Submission package when a GWU
principal investigator is involved in an IND study as an investigator only.

V. **Investigator Brochures/Device Manuals – All Applicable Drug and Device Studies**

The GWU Medical IRB examines all Investigator Brochures (IBs) and/or device manuals
associated with investigational drug/device studies. This review provides the IRB with an
opportunity to adequately assess the risk/benefit ratio for subjects participating in the research.
Please note that depending on the type of study under consideration, i.e., sponsor-initiated vs.
investigator-initiated, there may or may not be a brochure/manual associated with the study.

VI. **Recruitment Materials – All Applicable Studies**

The GWU Medical IRB reviews and approves all recruitment materials to be used by the PI to
contact subjects directly, or indirectly via other individuals. These documents include invitational
letters, advertisements, posters, flyers, press releases, etc. **Hard copy recruitment materials that
are NOT professionally produced must contain a GWU IRB stamp of approval (e.g., GWU
produced flyers, posters, etc.). Recruitment materials to be added to a website must contain a
statement that the GWU IRB has approved the recruitment advertisement.**

IRB approval for such subject recruitment materials lasts indefinitely or until the material(s) is
modified. Please note that recruitment for a particular study may not begin until the recruitment
process has been reviewed and approved by the GWU Medical IRB.

Subject recruitment materials should not be coercive and should not make any claims or
suggestions implying that the research will result in a favorable outcome or other benefit(s)
beyond what is outlined in the protocol and informed consent document, if applicable. This
limitation is especially critical when research involves subjects who are likely to be vulnerable to
undue influence. If recruitment material does make such claims, the GWU Medical IRB will not
approve it. If possible, the PI should limit recruitment materials to the following:

- The name of the PI and contact information, including the name of GWU;
- A simple and concise description of the purpose of the research;
- General eligibility criteria for participation;
- A truthful description of the possible benefits, which may result from participation in the
  research, if any;
- If there are no benefits, indicate whether subjects are paid for their participation or receive
  free treatment; and
- For studies recruiting minors, state that parental consent is required for participation.

Moreover, recruitment materials for investigational drug, device, or biologic studies should not
use terms such as “new treatment” “new medication” or “new drug” without explaining that the
test article is investigational in nature, i.e., not yet approved by the FDA for the intended use
under study. FDA believes that a phrase such as “receive new treatments” may lead subjects to believe that they will receive a new improved product that is effective for its use.

PIs should include proposed recruitment materials with the initial IRB Submission Package. If the material is not ready at the time of initial submission, PIs may submit the material as a modification to an already approved project. Requests for approval of recruitment materials following initial GWU Medical IRB approval of the protocol may qualify for expedited review. See Chapter 6 for further information regarding modifications to previously approved research.

VII. Data Gathering Instruments – All Applicable Studies

The GWU Medical IRB reviews and approves all data gathering instruments such as surveys, questionnaires, etc. to be used by the PI to obtain information/data from subjects. IRB approval for such instruments lasts indefinitely or until the instrument(s) is modified. Thus, if you propose to modify an already approved data-gathering instrument, you must submit a modification request to the GWU Medical IRB.

As with recruitment material, PIs should submit such instruments along with the initial IRB Submission Package, including draft versions of study instruments. **Do not use data gathering instruments until the GWU IRB has reviewed and approved the use of such instruments, unless the study is approved to design such questionnaires/instruments. If you have used data gathering instruments that have not been IRB reviewed and approved, the data gathered as a result of use of such instruments is invalid and must be excluded from data results.**

VIII. Informed Consent - All Applicable Studies

Prior to enrolling any subject in a research study, all investigators must **prospectively** obtain the legally effective, **written** informed consent of the individual or the individual’s **legally authorized representative** (LAR) unless the GWU Medical IRB has:

- Granted Exemption from IRB Review status to the research study;
- Specifically waived the requirement for obtaining written documentation of informed consent (e.g., approved verbal or telephone consent); or
- Specifically waived or altered the informed consent process.

Please refer to Chapter 4 for detailed guidance regarding informed consent.

IX. Research Subject Authorization Form – All Applicable Studies

As you are aware, the research related provisions of the HIPAA Privacy Rule have changed the way PIs conduct human subject research involving protected health information (PHI). PHI is defined as “individually identifiable health information” (IIHI) that has been created or received by a covered entity. IIHI is health information and associated demographic (identifying) information that either identifies an individual (“identified” information), or could reasonably be used to identify an individual (“identifiable” information).
A covered entity is defined as a healthcare clearinghouse, health place, or health care provider if the person 1) provides health care, 2) is paid for providing health care, and 3) the provider’s payment for health care involves the electronic transmission of health information. At GWU, the MFA and the University Hospital (UHS) are separate institutional covered entities. The entire workforce of the MFA and UHS is part of each institution’s respective covered entity.

As a general rule, all human subjects enrolled in research protocols after April 14, 2003, that involve PHI must sign a Research Subject Authorization Form (RSAF) that has been approved by the GWU IRB. This form is available at the GWU Office of Human Research website at http://www.gwumc.edu/research/forms.htm. The RSAF must specify all uses and disclosures of PHI that will be used or disclosed in the study. In some limited situations, the GWU IRB may approve a waiver of research subject authorization for research involving participation of live human subjects.

For additional information regarding RSAFs or the criteria for waiver thereof, please refer to Chapter 9 of this Manual.
CHAPTER 4: INFORMED CONSENT

This chapter provides: (1) guidance regarding what considerations a PI must take into account when drafting an informed consent document and subsequently engaging in the process of obtaining informed consent from a subject; (2) a summary of the considerations the IRB takes into account when reviewing a proposed informed consent document and ultimately approving such a document; and (3) guidance regarding when informed consent (written or otherwise) can be waived or altered by the GWU Medical IRB in accordance with federal regulations.

I. Process

The informed consent process is a way of ensuring that human subject research satisfies ethical principles. Informed consent is not only the signing of a document; rather it is an on-going educational process of disseminating information, both orally and in writing, to an individual (or his/her legally authorization representative (LAR) in accordance with applicable federal and/or governing state law of the state where informed consent is being obtained) in a clear and comprehensive manner so that the individual can choose whether to participate or continue to participate in a research study. Thus, PIs have an ongoing duty to inform subjects of any new information that might affect the subject’s willingness to continue participation in the study. Please refer to the end of this chapter for further guidance regarding when new information must be shared with already enrolled subjects.

The individual being asked to participate in the research study must not experience any form of duress, coercion, deceit, force or undue inducement. Therefore, PIs may seek consent only under circumstances that provide the prospective subject or his/her LAR sufficient opportunity to consider whether to participate and that minimize the possibility of coercion or undue influence.

In deciding what information should be disclosed in the informed consent process, the GWU Medical IRB views the proposed study from the perspective of the prospective subject by asking questions the subject might want to know before deciding to participate in the research. All information that might influence the decision of any reasonable person to participate in a particular study should be included in the informed consent form. For example, the risk of death from cardiac catheterization might be small, and, therefore, seem unimportant to a PI, but the risk may appear large to people asked to undergo the procedure for the benefit of others.

Moreover, the GWU Medical IRB will do what it can to enhance the prospective subject's comprehension of the information presented. The GWU Medical IRB will consider the nature of the proposed subject population, the type of information to be conveyed, and the circumstances under which the consent process will take place (e.g., manner, timing, place, personnel involved). After considering the issues, the IRB may suggest changes in the timing or location of a PI's first contact with potential subjects or changes in how others contact subjects during or following the study. Moreover, depending on the study population, the IRB may require the PI to administer a survey/test to potential subjects to determine whether the subjects understand the informed consent document prior to signing such a document. Finally, the GWU Medical IRB ensures that subjects are informed about who will have access to their study data and who might contact them. This point is especially important for subjects consenting to participate in multi-center studies.
Sometimes the information given to prospective subjects is so complex or possibly disturbing that it may require some time for it to be absorbed and understood. In these circumstances, the GWU Medical IRB may suggest that the PI either present the information and discuss the issues with prospective subjects on more than one occasion, or that a period of time elapse between providing the information and requesting a signature on the consent form. During this waiting period, prospective subjects might be encouraged to discuss their possible participation with family members, or close friends. Other approaches to communicating complex information may include the use of audio-visual materials, brochures, etc.

II. Contents

Federal regulations (21 CFR Part 50 and 45 CFR Part 46) require that the following information, at a minimum, be provided to each prospective subject or the prospective subject’s LAR prior to enrolling into a study unless the GWU Medical IRB determines that a waiver of or alteration to informed consent may be granted for a particular study:

- **Purpose of the Study.** A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject’s participation in the research, a description of the procedures to be followed, and identification of any procedures that may be experimental;

- **Potential Risks or Discomforts.** A description of any reasonably foreseeable risks or discomforts to the subject. Such risks/discomforts include physical risks as well as breach of confidentiality risks;

- **Anticipated Benefits.** A description of any benefits to the subject or to others which may be reasonably expected from the research;

- **Disclosure of Alternative Procedures.** A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;

- **Confidentiality of Records.** A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;

- **Compensation and Injury Explanation.** For research involving more than minimal risk, an explanation as to whether any compensation will be provided 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 obtained;

- **Contact Information.** An explanation of whom to contact for answers to pertinent questions about the research and research subject’s rights, and whom to contact in the event of a research-related injury to the subject; and

- **Voluntary Participation Statement.** A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

In addition, federal regulations provide that the following information be provided to subjects, where appropriate:
• 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 or the subject could make a woman pregnant) that is 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 subject¹; and
• The approximate number of subjects involved in the study.

Please access the GWU IRB Sample Informed Consent Form at http://www.gwumc.edu/research/human/forms/medical/Guidelines%20for%20Writing%20Informed%20Consent%20Forms.doc. This sample form includes all the information outlined above as well as additional information that the GWU Medical IRB prefers. The sample form also explains the format that the IRB finds acceptable. Keep in mind that this is a sample, so use your best judgment as to what is applicable and appropriate for your particular study.

A glossary of lay terms for use in preparing consent forms for human subjects can be found at a website maintained by University of California at Davis: http://ovcr.ucdavis.edu/HumanSubjects/HSDefinitions/HSGlossary.htm

For additional information regarding informed consent, please access the OHRP Informed Consent Checklist – Basic and Additional Elements at http://www.hhs.gov/ohrp/humansubjects/assurance/consentckls.htm.

III. Expression

All informed consent information, as outlined above, must be written in language that is understandable to the subject or his/her LAR. As a general rule, federal guidelines recommend that ICFs be written at an eighth grade level. However, if prospective subjects include children or populations with an average reading level that is below the 8th grade reading level, the GWU Medical IRB will take special care to ensure that both oral presentations and consent forms are comprehensible to all subjects. In these cases, ordinary language should replace technical terms (e.g., upper extremities should be referred to as arms, venipuncture - blood from your arm with a needle, etc.).

The GWU Medical IRB makes every effort to ensure that information is presented to prospective subjects in language they can understand. Thus, if an investigator proposes to enroll only English speaking subjects into a study, then the informed consent document will be in English. Alternatively, if an investigator proposes to enroll only non-English speaking subjects into a study, then the informed consent document shall be in the non-English language that is understandable to the subjects. In such a situation, the investigator must include 3 versions of the

¹ Please refer to Chapter 4, Section VI for the GWU CHR IRB Policy Regarding When Significant New Findings Developed During the Course of the Research Must be Provided to Subjects.
informed consent form (or information sheet) as part of the IRB submission package. The 3 versions include (1) an English version of the applicable documents referenced above; (2) a translated version of the English applicable documents into non-English; and (3) a back-translated version of the applicable non-English document into English along with the Translator/Back-Translator Form. The form is available at: http://www.gwumc.edu/Research/human/forms/sample/Translator%20and%20Backtranslator%20Form.doc

IV. Use of Exculpatory Language

The informed consent process may not contain exculpatory language through which the subject or LAR is asked to waive or appear to waive any of their legal rights, or release or appear to release the PI, sponsor, institution, or agents from liability for negligence. Examples of unacceptable exculpatory language include the following:

• By agreeing to this use, you should understand that you give up all claims 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 or sponsor 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.

Examples of acceptable language include the following:

• 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.
• The PI, GWUMC, MFA, or GWU 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.
• The PI, GWUMC, MFA, or GWU 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.

V. Modifying the Informed Consent Process

As stated above, the written informed consent process is the basic method for ensuring that ethical principles are followed for research involving human subjects. Given the importance of this process, federal regulations only allow for the waiver of or alteration to all or part of the informed consent process under very limited circumstances. Modifications to the informed consent process include the following: (1) waiver of documentation of written informed consent; (2) waiver of or alteration to all or part of the informed consent process; and (3) waiver of informed consent in
emergency research. Given that each of these modification options involves different criteria, there is oftentimes confusion among PIs regarding which modification option is most appropriate for his/her study. The following guidance clarifies the federal regulations governing the various modifications to the informed consent process.

A. Waiver of Documentation of Written Informed Consent

Under certain circumstances, the GWU Medical IRB may waive the requirement that some or all subjects or LARs sign an informed consent form. A waiver of written informed consent does not eliminate the requirement to obtain the verbal informed consent of the subject or the subject’s LAR. This verbal consent process should include all of the basic and additional elements, when appropriate, of informed consent. Whenever a PI requests waiver of written documentation of informed consent, the PI shall submit a written script of the information that will be provided/presented (orally) to potential subjects. This written script is often referred to as an Information Sheet.

In accordance with federal regulations, the GWU Medical IRB may waive the requirement to obtain written informed consent from some or all of the subjects if one of the following circumstances exists:

- The ICF document is the only record linking the subject with the research and the principal risks associated with this link would be potential harm resulting from a breach of confidentiality concerning the subject's participation in the research (e.g., studies on sensitive topics such as drug abuse or sexual deviance). If a waiver of written informed consent is based on this criteria, each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern;
- The research presents no more than minimal risk and involves procedures that do not require written consent when they are performed outside of a research setting; or
- The research activities are limited to the use of telephone or Internet questionnaires, surveys, etc. In this instance, the required elements of informed consent should be included in an Information Letter, which will include a statement to the effect that completion of the questionnaire constitutes consent to participate in the study.

B. Waiver of or Alteration to All or Part of the Informed Consent Process For Minimal Risk Studies

In accordance with the Common Rule regulations, the GWU Medical IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent provided that the GWU Medical IRB finds and documents that the waiver of or alteration to relates to one of the following types of research. Please note that, unlike the Common Rule, FDA regulations do not permit modifications or waivers of informed consent requirements except for emergency research. Thus, if you plan to conduct a minimal risk study that is subject to FDA oversight, e.g., a protocol designed to study the safety and effectiveness of a drug, device, etc., then waiver/alteration of ICF is not appropriate except for emergency research protocols. See the next section for guidance on Waiver of Informed Consent in Emergency Research.
1. Research Qualifying for Waiver/Alteration of the Informed Consent Process

Per 45 CFR 46.116(c), research conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine:

- Public benefit or services programs;
- Procedures for obtaining benefits or services under those programs;
- Possible change in methods in (or alternatives to) those programs or procedures; or
- Possible changes in methods or levels of payment for benefits or services under those programs;
- The research could not practically be carried out without the waiver or alteration.

45 CFR 46.116(d) - Research that involves no more than minimal risk to subjects and

- Waiver or alteration will not adversely affect the rights and welfare of the subjects;
- Research could not practically be carried out without the waiver or alteration; and
- Whenever appropriate, the subjects will be provided with additional pertinent information after participation in the study.

2. IRB Action on Research Qualifying for Waiver/Alteration to the Informed Consent Process

a. Waiver of Written Documentation of Informed Consent

To be considered for such a waiver the PI must check off on the IRB Submission Form that “request for waiver of written documentation of informed consent.” In addition, the PI must complete Part I of the Waiver of or Alteration to Informed Consent Request Form. Part I of this form provides the criteria for requesting waiver or written documentation of informed consent. Moreover, along with the request for waiver of written informed consent the PI shall submit a written script of the information that will be provided/presented (orally) to potential subjects, either as an introductory letter or information sheet.

b. Waiver of or Alteration to the Informed Consent Process

To be considered for a such a waiver or alteration, the PI must check off on the IRB Submission Form “request for waiver of or alteration to the informed consent process” and complete Part II of the Waiver of or Alteration to Informed Consent Request Form. Part II of this form provides the criteria for requesting a waiver of or alteration to the informed consent process.

C. Waiver of Informed Consent In Emergency Research
Both Common Rule (45 CFR 46.101(i)) and FDA regulations (21 CFR 50.24) allow PIs to enroll certain subjects\(^2\) without their legally effective informed consent or that of their legally authorized representative (LAR) in emergency research protocols that are designed to evaluate emergency care interventions provided that the conditions outlined below are met. PIs wishing to conduct research in an emergency setting involving more than minimal risk, but for which participation in the research holds out the prospect of direct benefit to the subject, should carefully review the information below to make sure that the proposed research qualifies for a waiver of informed consent in emergency research. In addition, PIs are encouraged to consult with the Chair of the GWU Medical IRB and/or members of OHR when preparing an IRB submission that involves waiver of informed consent in emergency research. What follows is a summary of the major points that need to be considered and discussed when such protocols are to be conducted at GWU.

According to FDA regulations, 21 CFR 50.24(a), the GWU Medical IRB may approve, initially and at continuing review, a study involving critical care research without requiring that informed consent of the research subjects be prospectively obtained if the GWU Medical 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 in the proposed protocol:

- Prospective subjects are in a life-threatening situation (diseases or conditions where the likelihood of death is high unless the course of the disease or condition is interrupted, e.g., myocardial infarction); available treatments are unproven or unsatisfactory; and the knowledge to be gained from the study will be used to determine the safety and effectiveness of the intervention being studied;
- Informed consent is not feasible because the subject cannot consent due to their medical condition, the intervention under investigation must be administered before consent from the subject's LAR is feasible, and subjects likely to be eligible for participation in the clinical investigation cannot be prospectively identified;
- Participation in the research may directly benefit the subject because subjects are facing a life-threatening situation that necessitates intervention; appropriate animal and other pre-clinical studies have been conducted and the information derived from those studies and related evidence support the potential of providing a direct benefit to individual subjects; and the risks and benefits of the experimental treatment are reasonable compared to those associated with the patient's medical condition and standard therapy;
- The clinical investigation could not practicably be carried out without the waiver of informed consent. If the GWU Medical IRB finds that research can be practicably carried out using consenting subjects or LARs, then the research shall be conducted with consenting subjects only;
- The PI has clearly defined the length of the potential therapeutic window based on scientific evidence and has committed to attempt to contact a LAR for each subject within the clinical investigation's therapeutic window and, if feasible, ask for consent within that window rather than proceeding without consent. The PI must summarize efforts made to

\(^2\) FDA regulations allow for this exception from informed consent for all subjects; however the HHS regulations limit the scope of this exception in that it does not apply to research involving fetuses, pregnant women, human in vitro fertilization and research involving prisoners.
contact LARs and make this information available to the IRB at the time of continuing review; and

- The IRB has reviewed and approved informed consent procedures and an informed consent document for situations in which consent of a subject or a legally authorized representative is feasible.

Additional protections of the rights and welfare of the subjects include:

- Prior to initiating the study, consult with representatives from the community from which subject will be drawn and obtain input from such representatives. Requests for meetings regarding the study can occur via newspapers, institutional newsletters, advertisements, local radio stations, at meetings, etc;
- Prior to the initiation of the investigation, public disclosure to the communities in which the clinical investigation will be conducted of the possible risks and expected benefits (e.g., relevant information from investigator's brochure, the informed consent document, and investigational protocol);
- Public disclosure of sufficient information following completion of the investigation to inform the community and researchers of the results of the investigation;
- Establishment of an independent data safety monitoring committee/board (DSMB) to exercise oversight of the investigation; and
- If consent is not feasible and a LAR is not available, the investigator must provide an opportunity for a family member to object to the subject's participation in the investigation within the therapeutic window, if feasible.

Pursuant to 21 CFR 50.24 (b), the GWU Medical IRB is responsible for ensuring that procedures are in place to inform each subject, at the earliest feasible opportunity, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. In the event that the subject remains incapacitated, either a the LAR of the subject, or if such a representative is not reasonably available, a family member must be informed of the same relevant information regarding the subject’s inclusion in the clinical investigation. In the same manner, the GWU Medical IRB must ensure that there is a procedure to inform the subject (or their LAR, or if none is reasonably available, a family member) that s/he may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

If a LAR 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 possible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a LAR or family member can be contacted, information about the clinical investigation is to be provided to the subject's LAR or family member, if feasible.

In accordance with 21 CFR 50.24 (c), any GWU Medical IRB determinations regarding proposed waiver of informed consent in emergency research protocols are to be retained by the IRB for at least 3 years after completion of the study and records of such studies are to be made accessible for inspection by the FDA.
In accordance with 21 CFR 50.24 (d), the GWU Medical IRB must ensure that there is an investigational new drug application (IND) or investigational device exemption (IDE) for all protocols involving a waiver of informed consent requirements for emergency research.³

According to 21 CFR 50.24 (e), if the GWU Medical IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under 21 CFR 50.24(a) or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the PI 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 IRBs which have been, or are asked to review this or a substantially equivalent investigation by that sponsor.

VI. Re-Consenting of Already Enrolled Subjects

Whenever significant new findings are developed during the course of a research study (e.g., additional risks have been identified) or less significant information regarding a modification to the study has occurred since subjects initially consented, such new findings/modified information must be provided to all enrolled subjects. A new finding is considered significant when the PI, sponsor, and/or GWU IRB concludes that the new finding would have been relevant to the subjects at the time of initial consent. Significant new findings include, but are not limited to, additional serious side effects, risks, potential benefits, and/or requirements or alternatives to the research study. Less significant information regarding a modification to the study could include change in membership of the research team, a change in the length of follow-up, etc. The GWU IRB, in consult with the PI, will decide which option (ICF addendum vs. modified ICF vs. information sheet) is most appropriate, given the circumstances.

A. Significant New Findings Developed During a Study

Significant new findings developed during the course of a study must be communicated to all subjects who previously consented. This communication takes place via a re-consenting process using either an addendum to the initial informed consent form (ICF addendum) or a modified ICF that includes the significant new findings. An ICF addendum informs currently enrolled subjects of ONLY the new/modified information relating to a study whereas a modified ICF informs currently enrolled subjects of ALL of the information relating to a study, i.e., it includes the language of the original ICF plus the new/modified information. Please note that both the ICF addendum and the modified ICF require the signatures of the subject (or subject’s LAR), the person obtaining consent, the witness (if applicable), and the PI.

B. Less Significant Information Regarding Modifications to a Study

³ Please note that there must be a separate IND or 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 21 CFR section 312.30 or 812.35.
Less significant information regarding modifications to a study must be communicated to all previously consented subjects. This communication takes place via a re-consenting process consisting of either an ICF addendum (defined above) or an Information Sheet. In this situation, an information sheet includes a written script of the modified ICF information that is provided/presented to subjects. Unlike the ICF addendum or modified ICF, an information sheet does not require any signatures.

For specific guidance regarding how to write an ICF addendum, please refer to the Sample ICF Addendum, which can be accessed at [http://www.gwumc.edu/research/forms.htm](http://www.gwumc.edu/research/forms.htm)
CHAPTER 5: SPECIAL CLASSES OF SUBJECTS

Federal regulations require all IRBs to give special consideration to protecting the following vulnerable subjects: pregnant women, fetuses, and neonates; prisoners; and children/minors. These special considerations are set forth in 45 CFR Part 46 as follows: Subpart B provides specific provisions for research involving pregnant women, fetuses and neonates; Subpart C sets out specific provisions for research involving prisoners; and Subpart D provides the specific provisions relating to research involving children. In addition, although not specified in regulation, but rather federal guidance, IRBs are strongly encouraged to give special consideration to protecting cognitively impaired individuals as well as students involved in research. Section I of this chapter summarizes federal regulations governing special subject classes and section II summarizes the special considerations taken into account when research involves cognitively impaired subjects or students.

I. Federal Regulations Governing Special Subject Classes

A. Research Involving Pregnant Women and Fetuses (45 CFR 46.204)

Pursuant to 45 CFR 46.204 pregnant women or fetuses may be involved in research if all of the following conditions are satisfied:

1. Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on non-pregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses;

2. 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;

3. Any risk is the least possible for achieving the objectives of the research;

4. The informed consent of the pregnant woman is obtained in accordance with the regulatory provisions for informed consent if the research holds out (i) the prospect of direct benefit to the pregnant woman, (ii) the prospect of a direct benefit to both the pregnant woman and the fetus, or (iii) 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 that cannot be obtained by any other means;

5. The informed consent of the pregnant woman and the father are obtained in accordance with the provisions for informed consent if the research holds out the prospect of direct benefit solely to the fetus except 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;

6. Each individual providing consent under paragraph (4) or (5) above is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; and

7. For children who are pregnant, assent and permission are obtained in accord with 45 CFR Part 46 Subpart D, see section F of this chapter for further guidance.

In addition to the above requirements, when considering research involving pregnant women or fetuses, the GWU IRB must ensure that the following conditions are also satisfied:

- No inducements, monetary or otherwise, are offered to terminate a pregnancy;
- Individuals engaged in the research have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and
- Individuals engaged in the research have no part in determining the viability of a neonate.

B. Research Involving Neonates (45 CFR 46.205)

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 section I.A.4 and 5 above is fully informed regarding the reasonably foreseeable impact of the research on the neonate;

3. Individuals engaged in the research have no part in determining the viability of a neonate; and

4. The requirements below are also met, as applicable.

Research Involving Neonates of uncertain viability. Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research unless the IRB determines that the following additional conditions have been met:

1. 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 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 LAR is obtained in accord with the
regulatory provisions for informed consent, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest.

**Research Involving Nonviable Neonates.** Nonviable neonates may not be involved in research 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 the regulatory provisions for informed consent, except that the waiver/alteration provisions of such informed consent 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, except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a LAR of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph.

**Research Involving 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 provisions of 45 CFR Part 46 Subpart D governing children/minors.

**C. Research Involving After Delivery, the Placenta, the Dead Fetus or Fetal Material (45 CFR 46.206)**

Research involving, after delivery: the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with applicable Federal or District laws and regulations regarding such activities.

If information associated with material described above is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of 45 CFR Part 46 are applicable.

**D. Research Not Otherwise Approvable (45 CFR 46.207)**

Research that the GWU IRB believes does not meet the requirements of 45 CFR 46.204 or 46.205 may nevertheless be approved, but only if:
1. The GWU 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 pregnant women, fetuses or neonates; and

2. The Secretary of HHS, after consultation with a panel of experts in pertinent disciplines (e.g. science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined that either:

   a. The research in fact satisfies the conditions of 45 CFR 46.204, as applicable; or
   b. The following:

      i. The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates;
      ii. The research will be conducted in accord with sound ethical principles; and
      iii. Informed consent will be obtained in accord with the informed consent provisions of the Common Rule (45 CFR Part 46; Subpart A) and other applicable subparts under 45 CFR Part 46.

E. Research Involving Prisoners – 45 CFR Part 46, Subpart C

45 CFR Part 46, Subpart C provides special protections for research involving prisoners, who, due to their incarceration (e.g., civil confinement in a mental facility or criminal confinement in a penal institution) may have limited ability to make truly voluntary decisions about whether to participate as subjects in research. Given this limited ability, no prisoner may be involved in human research unless the GWU IRB is appropriately constituted to review such research and the requirements outlined below are addressed by the PI and approved by the full IRB. Please be aware that these requirements apply to research that specifically targets prisoner populations as well as research involving non-incarcerated persons, one or more of which subsequently becomes a prisoner. Thus, if a subject becomes a prisoner after enrollment in a research study the PI must immediately notify the GWU IRB. At this point, the PI must decide whether s/he wishes to withdraw the subject prisoner from the protocol or keep the subject prisoner in the study. If the PI elects to withdraw the subject prisoner from the study, the subject prisoner must be informed of the reason for this action. Alternatively, if the PI elects to keep the subject prisoner in the study, the GWU IRB must, at the earliest opportunity re-review the research protocol and consent form in accordance with the requirements listed below. Pending this IRB re-review and approval, all interactions with the subject prisoner must cease. The GWU IRB has the ultimate authority to approve the involvement of the prisoner subject or determine that the subject must be withdrawn.

1. Composition of IRB When Reviewing Protocols Involving Prisoners as Subjects

   When an IRB reviews a protocol involving prisoners as subjects, the composition of the IRB must satisfy the following requirements. These requirements must be satisfied 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.

a. A majority of the IRB (exclusive of prisoner members) shall have no association with the prison(s) involved, apart from their membership on the IRB; and

b. At least one member of the IRB must be a prisoner, or a prisoner advocate with appropriate background and experience to serve in this capacity (e.g., former prisoner). 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 prisoner perspective. Please note that in a protocol involving prisoners as subjects is to be reviewed by more than one IRB, only one IRB must satisfy the requirement that at least one member of the IRB be a prisoner or a prisoner representative.

Whenever the IRB roster is changed to include a prisoner or a prisoner representative, the IRB must notify OHRP of this change.

2. Requirements for Involving Prisoners in Human Subject Research

When the GWU IRB reviews a protocol in which a prisoner is a subject, the IRB must document the following 7 findings in addition to other requirements:

a. The research falls under one of the following 4 categories of research:

   i. Studies (involving no more than minimal risk\(^4\) or inconvenience) of the possible causes, effects, and processes of incarceration and criminal behavior;

   ii. Studies (involving no more than minimal risk or inconvenience) of prisons as institutional structures or of prisoners as incarcerated persons;

   iii. Research on particular conditions affecting prisoners as a class (providing the Secretary of HHS has consulted with appropriate experts and published the intent to support such research in the Federal Register); or

   iv. Research involving practices that have the intent and reasonable probability of benefiting the prisoner subject. If the research involves possible assignment to a control group that may not benefit from the research, the Secretary of HHS must also consult with appropriate experts and publish the intent to support the research in the Federal Register (45 CFR 46.306).

b. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared with the general living conditions, medical care, medical, dental or psychological examination of healthy persons. Minimal risk in prisoner research is defined as 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.

\(^4\) The definition of minimal risk for research involving prisoners differs from the definition of minimal risk in the Common Rule. For research involving prisoners, the definition of minimal risk requires reference to physical or psychological harm, as opposed to harm or discomfort, to risks normally encountered in the daily live, or routine medical, dental or psychological examination of healthy persons. Minimal risk in prisoner research is defined as the probability and magnitude of physical or psychological harm that is normally encounters in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons.
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;

c. The risks involved in the research are commensurate with risks that would be accepted by non-prisoner volunteers;

d. Procedures for selecting 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;

e. The information is presented in language that is understandable to the subject population;

f. 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

g. 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 prisoner’s sentences, and for informing participants of this fact.

3. Permitted Research Involving Prisoners

For research involving prisoners, the following 2 actions must occur:

a. The institution engaged in the research must certify to the Secretary of HHS (through OHRP) that the IRB has reviewed and approved the research under 45 CFR 46.305; and

b. The Secretary (through OHRP) determines that the proposed research falls within one of the permissible 4 categories or research outlined above.

For additional guidance on the Involvement of Prisoners in Research, please go to www.//ohrp.osophs.dhhs.gov/humansubjects/guidance/prisoner.htm

F. Research Involving Children - 45 CFR Part 46, Subpart D

Pursuant to federal regulations, special considerations must be taken into account when proposed research involves minors. Under District of Columbia law, minors are defined as any individual less than 18 years of age who has not been legally declared emancipated. If a subject under the
The age of 18 is legally declared emancipated, s/he may consent to participate in research without the permission of a parent or guardian, e.g., no special rules regarding human subject research apply.

The PI and GWU Medical IRB must consider the following 3 items when reviewing research involving children/minors: (1) risk/benefit analysis; (2) parental permission; and (3) assent.

1. **Risk/Benefit Analysis**

   The GWU Medical IRB must classify research that involves children into one of four categories and document the resulting IRB discussions regarding the risks and benefits of the research study. The four categories of research involving children that may be approved by the GWU Medical IRB include the following:

   a. **Research Involving Not More Than Minimal Risk.** The GWU Medical IRB can approve such research if the PI obtains the written parental consent of at least one parent and the assent of the child. See 45 CFR 46.404. Research involving not more than minimal risk to a healthy child include urinalyses, obtaining small blood samples, EEGs, allergy scratch tests, minor changes in diet or daily routine, and/or the use of standard psychological or educational tests.

   b. **Research Involving Greater Than Minimal Risk and Prospect of Direct Benefit.** The GWU Medical IRB can approve such research if the:

      i. Risk is justified by the anticipated benefit to the subjects;
      ii. Anticipated risk/benefit ratio is at least as favorable as alternative approaches; and
      iii. PI obtains the written parental consent of at least one parent and the assent of the child.

      Examples of such research include biopsies of internal organs or spinal taps. Behavioral interventions, which may cause psychological stress may also fall within this category of research.

   c. **Research Involving Greater Than Minimal Risk, No Prospect of Direct Benefit, but the Study Could Yield Generalized Knowledge about the Child’s Disorder or Condition.** The GWU Medical IRB can approve such research if:

      i. Risk represents a minor increase over minimal risk;
      ii. The intervention/procedure presents experiences to children that are reasonable against those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
      iii. The intervention/procedure is likely to yield generalized knowledge about the child’s disorder/condition; and
iv. The PI obtains (1) the written parental consent of both parents if both parents have custody and are reasonably available; and (2) assent of the child. See 45 CFR 46.406

An example of a research protocol under this category could include the use of a drug in children when the risks to children have not yet been determined.

d. Research which does not meet any of the above criteria, but which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children. The GWU Medical IRB can approve such studies if:

i. 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

ii. The HHS Secretary, after consulting with a panel of experts in pertinent disciplines and following opportunity for public review and comments, has determined either:

(a) That the research in fact satisfies the requirements of 45 CFR 46.404, 405, or 406, as applicable, or

(b) Meets the following criteria:

• The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health and welfare of children;

• The research will be conducted in accordance with sound ethical principles; and

• The PI obtains (1) the written parental consent of both parents if they both have custody and are reasonably available; and (2) the assent of the child. See 45 CFR 46.407.

2. Parental Permission

**Parental permission** is the informed consent of the parent(s) to involve their children in human subject research. Thus, it should include all the information that is generally included in the GWU sample informed consent form. According to the federal criteria outlined above, parental permission from both parents is not required in all research situations; however, the GWU Medical IRB feels that whenever possible, the permission of both parents should be obtained. As a general matter, the PI should obtain both parents’ permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. Moreover, such written parental permission should be obtained before contacting children for participation in research.

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5 Both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.
3. Assent

In accordance with federal regulations, whenever a protocol involves minors capable of providing assent (e.g., capable of having a study explained to them and/or reading a simple assent form, and giving verbal or written assent if they decide to participate in the study) the PI must obtain both the child’s written assent as well as the written permission of the parents prior to enrolling such minors in a research study. Assent is an agreement by an individual who is not competent to give legally valid informed consent to participate in research. The assent process is said to assure “an element of understanding, cooperation, and a feeling of inclusion on the part of the child and also illustrates the investigator’s respect for the rights and dignity of the child in the context of research.”

The GWU Medical IRB has ultimate responsibility for making a determination as to whether a minor is capable of providing assent. In making this determination, the GWU Medical IRB takes into account the age, maturity, and psychological state of the child involved. The assent of the child is required in all research involving children except in the following situations:

(1) When the capability of some/all children is so limited that they cannot reasonably be consulted, or
(2) The intervention/procedure being studied holds out a prospect of direct benefit that is important to the health or well being of the children and is available only in the context of the research. If it is deemed appropriate that the child’s assent should be obtained, the GWU IRB should ensure that the assent form is tailored for the child, with respect to his or her level of understanding. For young children, especially, the assent form should be designed as a one-page document, with simple, age-appropriate language, and presented in a manner understandable to the child. See the table at end of this chapter.

The GWU Medical IRB general rules regarding assent are as follows:

a. Children 7 years of age or older, with normal intelligence, must be offered the opportunity to participate in the consent process and offered the opportunity to sign a form documenting his/her assent to participate;
b. Mere refusal to object cannot be construed as assent to participate; and
c. Reasonable efforts must be made by the PI to tailor the consent form for comprehension by the child participant.

To access a sample GWU assent form please click on http://www.gwumc.edu/research/human/forms/sample/Sample%20Assent%20Form.doc.
## Research Involving Children Table

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<tr>
<td><strong>No Greater Than Minimal Risk</strong></td>
<td>Assent of child and permission of at least one parent</td>
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</table>
| **Greater Than Minimal Risk & Prospect of Direct Benefit** | Assent of child and permission of at least one parent  
|                                           | Anticipated benefit justifies the risk                                                                                                         |
|                                           | Anticipated benefit is at least as favorable as that of alternative approaches                                                                |
| **Greater Than Minimal Risk & No Prospect of Direct Benefit** | Assent of child and permission of both parents  
|                                           | Only a minor increase over minimal risk                                                                                                         |
|                                           | Likely to yield generalizable knowledge about the child’s disorder or condition that is of vital importance for the understanding or amelioration of the disorder or condition. |
|                                           | The intervention or procedure presents experiences to the child that are reasonably commensurate with those in the child’s actual or expected medical, dental, psychological, social, or educational situations. |
| **Any Other Research**                   | Assent of child and permission of both parents  
|                                           | 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 |
|                                           | The HHS Secretary approves, after consultation with a panel of experts in pertinent disciplines (e.g., science, medicine, education, ethics, law) and following publication in the Federal Register and public comment |
II. Guidelines Governing Special Subject Classes

A. Cognitively Impaired Individuals

At times, PIs propose research involving a subject population for which some or all of the population may be unable to consent for themselves or their ability to consent for themselves is compromised. These subject populations may include unconscious patients, persons with Alzheimer's, patients with diagnosed psychoses, and those institutionalized as mentally disabled.

There are no federal regulations specific to research involving cognitively impaired persons. However, there are specific GWU Medical IRB policies that require that special criteria be followed to ensure that these subjects are protected from potential human subject research violations. One of these criteria involves the requirement that any PI proposing to conduct research on such populations provide in the protocol written, detailed justification for including such subjects in a study as well as a careful analysis of the relative risks and benefits of the study to the individual subject and to the particular group of subjects. In addition, the GWU IRB considers issues such as privacy and confidentiality and coercion and undue influence. Moreover, the GWU IRB may require the PI to administer a test to potential subjects to evaluate the subjects’ capacity to consent. Lastly, whenever research involves mentally compromised populations, the GWU Medical IRB expects that the research will bear some direct relationship to the conditions or circumstances of the subject population.

When research involving cognitively impaired individuals is approved, the GWU IRB requires additional safeguards (e.g., involvement of subject advocates, independent monitoring, formal capacity assessment, waiting periods) as part of the research plan to protect participants.

The National Bioethics Advisory Commission (NBAC) has issued 21 recommendations for IRBs, the research community, and Federal regulators to consider regarding the decision-making capacity of particularly vulnerable subjects. The complete report, “Research Involving Persons with Mental Disorders That May Affect Decision Making Capacity” (December 1998), can be found on-line at http://bioethics.gov/capacity/TOC.htm.

B. Students

Whenever the GWU IRB considers a study involving student subjects, the GWU IRB reviews the protocol to determine whether the study is designed in such a manner that the investigator has minimized the possibility of coercion of or undue influence on student subjects. If the GWU IRB finds that a study is designed to minimize the possibility of coercion of or undue influence on students, then the study will most likely be approved. As a general matter, the GWU IRB usually finds the following study designs to be approvable: (1) studies in which the instructor/investigator enrolls “other” students into a study, i.e., does not enroll his/her own students; (2) studies in which the instructor/investigator enrolls his/her own students, but the study is conducted anonymously; or (3) studies in which the instructor/investigator enrolls his/her own students, but recruitment is conducted by another instructor and data is blinded/coded before being shared with the instructor.
Alternatively, if the GWU IRB determines that a study involving students is designed in such a manner that the possibility of coercion of or undue influence on student subjects is not or can not be minimized, the GWU IRB will not approve the study unless the protocol is modified to minimize this possibility or the investigator provides justification for requiring such a study design and includes special protections for student subjects. An example of such a study is one in which the investigator is also the instructor of the students and the investigator recruits his/her own students and knows the identity of the subjects. Students involved in this type of study require special protections given the investigator/instructor’s knowledge of which students enrolled in the study and which students did not; it is believed that investigators/instructors may use this knowledge to give preferential treatment to those students who enroll in the study.

Points to consider when proposing a study involving student subjects:

- Unless otherwise justified, students must be given the opportunity to opt out;
- Investigators should not use class time for recruitment or to complete study questionnaires unless research is directly related to the class material;
- Investigators should not offer excessive extra credit or financial rewards as a way to entice students to enroll because doing so can be seen as form of coercion; and
- When appropriate, the GWU IRB may include a student in IRB deliberations or consult with a student when students are likely to be participating in research.
CHAPTER 6: IRB REVIEW OF RESEARCH

The GWU Medical IRB reviews all human subject research falling within its jurisdiction prior to: (1) the initiation of proposed research activities; (2) the expiration date of previously approved research; and (3) implementation of any proposed modifications to previously approved research, with certain exceptions. In accordance with federal regulations, GWU Medical IRB review of the activities identified above must be conducted in accordance with one of the following three categories of review:

1. Exempt from IRB Review (EX) (used for certain initial review studies);
2. Expedited Review (ER) (used for certain minimal risk initial studies, certain continuing review studies and minor modifications); or
3. Full Committee Review (FCR) (used for greater than minimal risk initial or continuing review studies and major modifications).

Section I of this chapter explains the categories of IRB review that are available for proposed research activities, i.e., EX, ER or FCR. Section I also provides information regarding the processes that are involved when a PI submits, and the GWU Medical IRB reviews, a new research protocol. Section II of this chapter explains the two categories of IRB review available for continuing review research activities, i.e., ER or FCR. Section II also provides information regarding the processes that are involved when a PI submits, and the GWU Medical IRB reviews, requests for continuing review of ongoing studies. Lastly, Section III of this chapter explains the two categories of IRB review available for proposed modifications to previously approved research, i.e., ER or FCR. Section III also provides information regarding the processes that are involved when a PI submits, and the GWU Medical IRB reviews, proposed modifications to previously approved research.

I. IRB Review of Proposed Research Activities

A. Types of Studies Eligible for Exempt from IRB Review

Pursuant to the Common Rule, only certain research activities can be found to be exempt from IRB review, including the requirement to obtain informed consent as well as continuing review. Please note, however, that pursuant to GWU Policy IRB review of research activities appearing to meet one or more of the exempt categories must nevertheless undergo IRB review to ensure consistent regulatory compliance. A specific listing of these research activities can be found in the Exempt from IRB Review Request Form found at http://www.gwumc.edu/research/forms.htm. Below you will find a detailed explanation of what types of studies qualify under exempt category (4).


Pursuant to 45 CFR 46.101(b)(4), research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, is exempt from the requirement for IRB review and approval, but only if the existing 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. Thus, in order to qualify for this exemption category, the data or specimens must be:

1. Existing **and** publicly available; or
2. Existing **and** unidentifiable.

Existing data or specimens is defined as data/specimens collected (i.e., on the shelf) prior to the time the study is submitted for IRB review. Thus, if a study involves data/specimens that have already been collected at the time of IRB review, as well as the prospective collection of data or specimens, then the study will not qualify as exempt under category 4, but could qualify for expedited review.

The term **publicly available** was intended to apply to public sources of data, such as death certificates, that are accessible to the public at large. It’s meaning with respect to human specimens is widely debated. There are many organizations/entities that make human cells/tissues broadly accessible to the research community at reasonable cost. Because these institutions offer specimens/materials to only a subset of the public at large, i.e., the research community, the materials are not considered publicly available. Thus, if you propose to obtain specimens from such an organization/entity, keep in mind that the GWU IRB has the final say (in consultation with OHRCTT) as to whether such specimens meet the definition of “publicly available."

**Identifiers**, whether considered direct (e.g., names, SSNs, pathology accession numbers) or indirect (e.g., codes), permit specimens to be linked to individual subjects. Thus, this exemption category applies to studies involving specimens where such personal information was never collected or was never made available to the researcher or his/her collaborator. For example, the exemption applies to studies involving specimens provided by a tissue bank or other repository, so long as the specimens are provided without identifiers.

Please note that this exemption generally does not apply in situations where a GWU researcher receives “coded” specimens from a non-GWU collaborator, if the collaborator keeps the key to the code, even though the GWU researcher may have no access to patient identities. OHRP has held that in such situations the information is considered identifiable because the research user, GWU researcher or non-GWU collaborator, could re-identify the subject and link the subject to the data/specimen based on the key that is maintained.

This policy is based on guidance provided by OHRP Human Subject Regulations Decision Charts, which can be accessed at [http://ohrp.osophs.dhhs.gov/humansubjects/guidance/decisioncharts.htm](http://ohrp.osophs.dhhs.gov/humansubjects/guidance/decisioncharts.htm) and on an NIH Brochure entitled “Research on Human Subjects,” which can be found at [http://www.cdp.ims.nci.nih.gov/brochure.html](http://www.cdp.ims.nci.nih.gov/brochure.html).

a. When to submit

Proposed studies eligible for exempt from IRB review are reviewed on a first-come, first-serve basis. Thus, PIs should submit protocols appearing to meet one of the exempt categories once an IRB submission package is complete. **PIs of such proposed exempt studies need not abide by the FCR submission deadlines because these deadlines apply only to studies/actions that require full committee consideration; proposed exempt studies are reviewed by the IRB Chair or designee; not the full committee.**

b. What to submit

A PI submitting a proposed study qualifying as exempt from IRB review should submit to OHR a complete IRB Submission Package consisting of 1 copy of all of the items of information, as applicable, listed on the Medical & Non-Medical IRB Submission Checklist, which can be accessed at [http://www.gwumc.edu/research/forms.htm](http://www.gwumc.edu/research/forms.htm). The complete IRB submission package is to be forwarded to OHR, 613 Ross Hall. **Submission of IRB correspondence, including IRB submission packages, to any other location, e.g., the office of the Chair of the GWU IRB, will only delay your review time.**

c. How the submission is processed

OHR staff will review the IRB Submission Package and make a preliminary determination as to whether the IRB submission package is complete and whether the study qualifies as exempt from IRB review. If it is determined that information is missing, the PI will be notified, via email (where possible) or telephone as to what information is still required. Once OHR staff makes a preliminary determination regarding whether a proposed study qualifies as exempt from IRB review, the AVP for OHRCTT will review the preliminary determination prior to forwarding the study onto the IRB Chair or designee(s) for concurrence. If the IRB Chair or designee concurs that the proposal qualifies as exempt from IRB review, a memorandum will be generated reflecting this decision. If, however, the IRB Chair or designee determines that the study does not qualify as exempt from IRB review the PI will be informed of this decision informally, either by phone or by email, by an OHR staff member. In this situation, an OHR employee will explain why a particular study does not qualify as exempt from IRB review, e.g., study involves a vulnerable population. The PI will be informed of what additional steps s/he must take in order to have his/her study reviewed by the GWU Medical IRB, either via expedited or full committee review procedures.

d. What to expect
GWU Medical IRB review of studies qualifying as exempt from IRB review will occur within 2 to 3 weeks from the date of submission of a complete IRB submission package to OHR. However, please keep in mind that this turnaround timeframe is dependent on the responsiveness of the PI and his/her research team to inquiries, if any. Once the IRB Chair or designee approves a proposed protocol as exempt from IRB review, the PI will receive an Exempt from IRB Review Letter. This letter will identify which exempt category his/her study qualifies under. This letter will not include a continuing review date due to the fact that exempt studies are not subject to continuing review. The only time that an Exempt from IRB Review study is subject to re-review by the Chair of the GWU Medical IRB or his/her designee is when the PI proposes modifications to the study initially categorized as exempt from IRB review. In such situations, the PI must prospectively inform the IRB Chair of such changes and obtain IRB approval of such changes before implementing them. The Exempt from IRB Review Letter will inform the PI of what to do if such modifications are proposed. Please note that a PI cannot begin a study until s/he receives an Exempt from IRB Review Letter.

In addition, this Exempt from IRB Review letter asks the PI to notify the GWU IRB when an exempt from IRB review study is completed, i.e., closed or terminated. The letter directs the PI to notify the GWU IRB of study completion via completion of the Continuing Review Data Collection and Project Termination Form, which can be located at http://www.gwumc.edu/research/forms.htm.

B. Expedited Review

The Common Rule, FDA regulations, and GWU IRB Policy allow for expedited review of certain categories of research activities that:

- Present no more than minimal risk to human subjects,
- Do not involve a special class/vulnerable population (See Chapter 5);
- Do not involve a sensitive subject matter (e.g., illegal drug use, alcohol abuse, sexual preferences, etc.); and
- Involve only procedures listed in one or more of the categories that constitute expedited review projects.

Such projects may be reviewed by the GWU Medical IRB through the expedited review procedures authorized by 45 CFR 46.110 and 21 CFR 56.110. An expedited review procedure consists of a review of research involving human subjects by the IRB Chair or by one or more designees from among members of the IRB.

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6 Please note that the definition of minimal risk is viewed differently for research involving vulnerable subjects, children and minors, prisoners, pregnant women and fetuses, cognitively impaired persons, traumatized and comatose patients, and the terminally ill. This issue is addressed more completely in the OHRP 1993 Guidebook for IRBs, Chapter 6: Special Classes of Subjects. A copy of this chapter is available upon request.
1. Types of Studies Eligible for Expedited Review

For a complete listing of the categories of research eligible for expedited review, please see the Expedited Review Request Form found at http://www.gwumc.edu/research/forms.htm.

The activities listed on the Expedited Review Request Form should not be deemed to be of minimal risk simply because they are included on that form. Inclusion on this form merely means that the activity is eligible for review through the expedited review procedure when the specific circumstances of the proposed research involve no more than minimal risk to human subjects. In other words, just because a proposed study is included on the Expedited Review Request Form does not necessarily mean the GWU Medical IRB will agree to review/approve it via expedited review procedures. Please keep in mind that the GWU Medical IRB has the final say in these situations. For instance, the GWU Medical IRB usually requires studies involving vulnerable populations to be reviewed by the full committee.

2. Processes Associated with Review of Research Qualifying for Expedited Review

a. When to submit

Proposed studies eligible for expedited review are reviewed on a first-come, first-serve basis. Thus, PIs should submit protocols appearing to meet one of the expedited review categories once an IRB submission package is complete. PIs of such proposed expedited review studies need not abide by the FCR submission deadlines because these deadlines apply only to studies/actions that require full committee consideration; proposed expedited review studies are reviewed by the IRB Chair or designee; not the full committee.

b. What to submit

A PI submitting a proposed study that may qualify for expedited review should submit to OHR a complete IRB Submission Package consisting of 1 copy of all of the items of information, as applicable, that are listed on the Medical & Non-Medical IRB Submission Checklist, which can be accessed at http://www.gwumc.edu/research/forms.htm. The complete IRB submission package is to be forwarded to OHR, 613 Ross Hall. Submission of IRB correspondence, including IRB submission packages, to any other location, e.g., the office of the Chair of the GWU IRB, will only delay your review time.

c. How the submission is processed

OHR staff will review the IRB Submission Package and make a preliminary determination as to whether the IRB submission package is complete and whether the study satisfies one (or more) of the expedited review categories. If it is determined that information is missing, the PI will be notified, via email (where possible) or telephone as to what information is still required. Once OHR makes a preliminary determination regarding
whether a proposed study qualifies for expedited review, the IRB Chair or designee will
review the preliminary determination. If the IRB Chair or designee determines that the
proposed research qualifies for expedited review, a memorandum will be generated
reflecting this decision. If, however, the IRB Chair or designee determines that the study
does not qualify for expedited review the PI will be informed of this decision informally,
either by a phone or by email, by an OHR staff member. In this situation, an OHR
employee will explain why a particular study does not qualify for expedited review. The
PI will be informed of what steps s/he must take in order to have his/her study reviewed
by the full GWU Medical IRB.

d. What to expect

GWU Medical IRB review of eligible expedited review studies should occur within 2 to 3
weeks from the date of submission of a complete IRB submission package to OHR.
Please note that this 2-3 week timeframe is dependent on the diligence of the PI and
his/her research team should revisions be requested. Once the IRB Chair or designee
approves a proposed protocol under expedited review procedures, the PI will receive a
Final IRB Approval Letter – Expedited Review. This letter will identify which expedited
review category(ies) his/her study qualified under. This letter also includes all the
conditions of approval for a particular study, including the next continuing review date.
Please note that a PI cannot begin a study until s/he receives a final IRB Approval Letter.

If the IRB Chair or designee determines that an eligible expedited review study is not
approvable, the PI will be informed of this decision via a memorandum. The
memorandum will inform the PI that the IRB Chair or designee has concluded that the
study is not approvable, but that the study will be re-considered by the full committee.
Pursuant to federal regulations, an expedited review study may only be disapproved after
consideration by the full IRB. Please see 45 CFR 46.110(b).

C. Full Committee Review (FCR)

1. Types of Proposed Research Studies Eligible for FCR

Protocols not qualifying as exempt from IRB review or for expedited review (e.g., greater
than minimal risk) must be reviewed by the full committee at a regularly convened
meeting.

2. Processes Associated with Review of Proposed FCR Research

a. When to submit – FCR submission deadlines

New protocols requiring FCR will be processed upon receipt of a complete IRB
submission package. Such protocols must be received by OHR no later than two weeks
prior to the next scheduled meeting of the full committee. As a general matter in order for
a study to be reviewed at the 2nd Tuesday IRB meeting, it must be received by OHR no
later than close of business on the 4th Tuesday of the previous month. In order for a study
to be reviewed at the 4th Tuesday IRB meeting, it must be received by OHR no later than
close of business on the 2nd Tuesday of that month. Please keep in mind that there are a maximum number of new protocol studies that can undergo FCR at each convened IRB meeting. Given this limitation, proposals are generally reviewed on a first come first serve basis.

Please note that new project submissions are assigned to a particular committee for review based on when the submissions are received by OHR. Therefore, when a study is assigned to one of the committees (either the second Tuesday or fourth Tuesday committee), all matters related to that project (e.g., revisions, reportable events, continuing review) are generally assigned to that same committee. However, when there are exigent circumstances that require a protocol to be reviewed as soon as possible, rather than await the next IRB meeting of the committee that originally reviewed it, then they study will be considered at the next scheduled IRB meeting.

b. What to submit

A PI submitting a proposed study qualifying for full committee review should submit to OHR a complete IRB Submission Package consisting of the appropriate number of copies of all of the items of information, as applicable, that are listed on the Medical & Non-Medical IRB Submission Checklist, which can be accessed at http://www.gwumc.edu/research/forms.htm.

c. How the submission is processed

OHR staff will review the IRB Submission Package and determine whether the package is complete. If it is determined that information is missing, the PI will be notified, via email or telephone, as to what information is still required. Once it is determined that the IRB Submission Package is complete, an OHR staff member will add the protocol to the next scheduled IRB meeting agenda, depending on when the package was submitted.

d. Assignment of FCR protocols

New protocols requiring FCR will be assigned to one primary reviewer and one secondary reviewer. These reviewers are provided with one copy of all the documents that were submitted by the PI, while the remainder of the committee is provided with one copy of each of the following, as applicable: IRB Submission Checklist, IRB Submission Form, FDA form 1572, protocol summary, informed consent/assent documents; research subject authorization form, advertising/recruitment material, data gathering instruments, faculty approved student research proposal; and site permission letter. These individuals also have access to additional information upon request.

The primary/secondary reviewers may request additional information from the PI prior to the meeting at which the proposed study is to be reviewed. The primary reviewer will present the proposed project to the other IRB members, along with any comments/concerns the reviewer may have relating to the study. The secondary reviewer will provide additional comments/concerns above and beyond those identified by the
primary reviewer. Following the primary/secondary reviewer comments/concerns, other IRB members are free to add their comments/concerns regarding the study. Following additional comments, if any, the full committee will discuss the project and bring it to a vote.

e. What to expect

GWU Medical IRB review/approval of new studies requiring FCR should occur within 4 to 6 weeks from the date of submission of a complete IRB submission package to the GWU Medical IRB. This turnaround time is dependent on the timing and substance of the submission package, as well as the responsiveness of the PI and his/her research team to outstanding issues identified by the IRB, if any. Once the full committee approves a proposed protocol, the PI will receive a Final IRB Approval letter – Full Committee Review. This letter will include all the conditions of approval for a particular study, including the next continuing review/renewal date. The next continuing review/renewal date is dependent on the level of the risk associated with the study, which is determined by the IRB members at the time the IRB considers the study for initial approval. Please note that a PI cannot begin a study until s/he receives a Final IRB Approval Letter.

II. Time Sensitive (New) Protocols

As a general rule, protocols requiring FCR must be received by OHR no later than two weeks prior to a scheduled IRB meeting in order to ensure that the assigned reviewers have ample time to conduct a thorough review of the study. The GWU Medical IRB understands, however, that there may be situations when a PI requires a quick IRB response due to extenuating circumstances that fall beyond his/her control. If a PI should experience extenuating circumstances that would require FCR of a protocol in a shorter than usual timeframe, please contact OHR to discuss your situation. OHR, in deliberation with the IRB Chair, will determine whether a protocol can be reviewed at the next scheduled IRB meeting regardless of submission date.

III. IRB Continuing Review of Ongoing Research Activities

All ER and FCR studies must undergo continuing review. IRB continuing review can occur via expedited review procedures or full committee review procedures, depending on the degree of risk associated with a given study. Pursuant to federal regulations, the following studies can undergo expedited review at continuing review time. If a study does not fall within one of the categories below, the study must undergo FCR.

1. Continuing review of research previously approved via expedited review procedures;
2. Continuing review of research previously approved by the full GWU IRB 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;
   (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.

3. Continuing review of research, not conducted under an investigational new drug application or investigational device exemption and the GWU Medical 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.

A. Processes Associated with Continuing Review of Ongoing Research Activities

1. When to submit

All studies undergoing continuing review, regardless of the type of review will be processed and reviewed upon receipt of a complete continuing review package. Such studies will be reviewed on a first come first serve basis. PIs are strongly encouraged to submit the requested continuing review information (outlined below) by the date provided in the Continuing Review Reminder Letter in order to avoid the possibility of automatic expiration of IRB approval of his/her study due to a lapse in continuing review. Submission of IRB correspondence, including continuing review information to any other location, e.g., the office of the Chair of the GWU IRB, will only delay your review time.

PIs of studies eligible for expedited continuing review need not abide by the FCR submission deadlines because these deadlines apply only to studies/actions that require full committee consideration; studies eligible for expedited continuing review are reviewed by the IRB Chair or designee; not the full committee.

2. What to submit

PIs submitting studies for continuing review should submit to OHR a complete continuing review package consisting of 1 copy (for studies qualifying for expedited review) or 15 copies (for studies requiring FCR) of the following information:

- The Continuing Review Reminder Letter;
- A completed Continuing Review Data Collection & Study Termination Form, with supporting documentation, as applicable;
- If the study is still actively enrolling subjects, an unstamped version of the most recently approved Informed Consent/Assent Form, as applicable; and unstamped version of the most recently approved Research Subject Authorization Form, as applicable.

For those studies in which the PI is asking for approval of modifications at the same time s/he is seeking continuing review approval, the PI should include as part of his/her continuing review package any documents that will need to be modified as a result of the proposed modifications, e.g., proposed modified informed consent/assent form, research subject authorization form, recruitment material, data-gathering material (e.g., surveys, questionnaires, etc.) and/or protocol, as applicable. If modifications are being proposed
for any of these documents, the PI must include a copy(ies) of the old version(s) with the changes highlighted and a copy(ies) of the new version(s) without highlights.

3. How the submission is processed

a. Continuing Review Information Submitted to the IRB Prior to or on Study Expiration Date

The GWU IRB will accept continuing review data collection forms and accompanying information that is submitted to the IRB prior to or on the study expiration date. The GWU IRB will consider this continuing review data collection form along with the information already contained in the IRB-maintained study file. The GWU IRB will rely on the above referenced information even if IRB continuing review approval is not obtained until after the study has expired. Please note that during the lapse in IRB approval period, the Principal Investigator is prohibited from engaging in any study related activities.

OHR staff will review any continuing review package received in OHR on or before the study expiration date and make a preliminary determination as to whether the package is complete. If it is determined that information is missing, the PI will be notified, via email, as to what information is still required. Additionally, OHR staff will make a preliminary determination regarding whether a continuing review study qualifies for expedited review. If it is determined that a study does qualify for expedited review, the IRB Chair or designee will review the preliminary determination. If the IRB Chair or designee determines that the continuing review research qualifies for expedited review, the IRB Chair or designee will review the following information:

- The completed Continuing Review Data Collection Form;
- For those studies actively enrolling subjects, a copy of the current informed consent/assent document and any newly proposed consent/assent document and a copy of the current research subject authorization form and any newly proposed research subject authorization form, if applicable, and
- A copy of, or be provided access to, the complete protocol including any modifications previously approved by the IRB.

When reviewing the current informed consent document, the IRB Chair or designee should ensure that the currently approved or proposed informed consent/assent/RSAF forms are still accurate and complete; and any significant new findings that may relate to the subject’s willingness to continue participation are provided to the subject.

When a continuing review study is scheduled for an upcoming IRB meeting, one reviewer (primary) will be assigned to review the continuing review study. The primary review will be provided with the same information that is outlined above and will be provided with access to copies of all IND and SAE forms that have been submitted to the SAE subcommittee since last continuing review. The primary reviewer may request additional information from the PI prior to the meeting at which the continuing review study is to be reviewed. In addition, all other IRB members will be provided with the protocol
summary; the completed Continuing Review Data Collection Form; and a copy of the current informed consent/assent/research subject authorization document(s) and any newly proposed versions of such document. At the scheduled meeting, the primary reviewer will present the continuing review project to the other IRB members. Following the presentation, other IRB members may add their comments/concerns regarding the study. After additional comments, if any, the full committee will bring the continuing review study to a vote.

b. Continuing Review Information Submitted to the IRB After Study Expiration Date

The GWU IRB will NOT accept continuing review information that is submitted to the IRB after a study has expired. The GWU will only review such a study if the PI submits a new IRB submission package, including a new IRB submission form, protocol, informed consent/assent form(s) (if applicable), research subject authorization form (if applicable), and all associated documents are reviewed and approved by the GWU IRB as a new study with a new IRB number.

4. What to expect

A PI can expect a response to a continuing review study qualifying for expedited review within 2 to 3 weeks from the date of submission of a complete continuing review submission package to OHR. This 2-3 week timeframe is dependent on the diligence of the PI and his/her research team should revisions be requested. Once the Chair or designee renews a continuing review protocol under expedited review procedures, a Continuing Review Letter with a new GWU IRB Stamped approval date will be forwarded to the PI. The PI will also receive any study related materials that require a new IRB approval date.

Alternatively, continuing review studies requiring FCR will be scheduled for the next upcoming IRB meeting. A PI can expect a response to his/her continuing review study within 4 – 6 weeks; depending on the timing of the submission of the continuing review study, the next scheduled IRB meeting, and the diligence of the PI and his/her research team should revisions be requested. Once the IRB approves a continuing review study, the PI will receive a Continuing Review Letter with a new GWU IRB Stamped approval date. The PI will also receive any study related materials that require a new IRB approval date.

IV. IRB Review of Modifications to Previously Approved Research

The GWU Medical IRB recognizes that modifications to protocols, e.g., study design, informed consent/assent documents, research subject authorization forms (RSAFs), recruitment material, and/or data gathering instruments may occur as the study progresses. Thus, requests for GWU Medical IRB approval of modifications to any aspect of a study may be requested at any time; however, please note that an IRB approval of a modification does not alter the original approval date or expiration date that has been assigned to the study, e.g., the next continuing review/renewal date.
The category of IRB review assigned to a proposed modification to a previously approved research study is dependent upon whether the original protocol was found exempt from IRB review or for those studies not considered exempt, whether the proposed modification is considered minor or major. The Chair of the GWU Medical IRB or his/her designee has final authority for making such determinations.

All proposed modifications to previously approved studies require review and approval by the GWU Medical IRB PRIOR TO implementing such changes except when a proposed change or amendment is necessary to eliminate apparent immediate hazards to research subjects. In such a situation, the GWU Medical IRB should be informed of the change in writing within 5 calendar days following its implementation. This is one of many GWU Medical IRB conditions of approval that is communicated to the PI via a final IRB approval letter.

A. Modifications to Studies Initially Categorized as Exempt from IRB Review

1. When to submit

Proposed modifications to previously approved exempt studies are reviewed on a first come first serve basis. PIs of such studies must submit proposed modifications prior to implementing such changes unless the proposed change is necessary to eliminate immediate hazards to subjects.

*PIs submitting proposed modifications to a previously approved exempt study need not abide by the FCR submission deadlines because these deadlines apply only to studies/actions that require full committee consideration; proposed modifications to previously approved exempt studies are reviewed by the IRB Chair or designee; not the full committee.*

2. What to submit

For modifications to studies initially categorized as Exempt from IRB Review, the PI must submit to the Chair of the GWU Medical IRB 1 copy of a memorandum outlining the modifications being proposed. Along with this memorandum, the PI should submit the following, as appropriate:

- If the modification affects the approved protocol - a copy of the original protocol with the requested modifications highlighted (now referred to as the modified protocol) and a non-highlighted modified protocol with a new version date; and/or
- If the modification affects previously approved recruitment materials – the modified recruitment materials; and/or
- If the modification affects previously approved data gathering instruments – the modified surveys/questionnaires, etc.

3. How the submission is processed

The OHR staff will review the proposed modification and any attached documentation and make a preliminary determination as to whether the proposed modification results in the
study no longer being considered exempt from IRB review. If it is determined that information is missing, the PI will be notified, via email, where necessary as to what information is still required. Once OHR makes a preliminary determination regarding the proposed modification, the IRB Chair or designee will review the preliminary determination. Following review of the preliminary determination, the IRB Chair or designee will make one of the following determinations:

- The proposed modification does not change the original “Exempt from IRB Review” determination. In this situation, the PI will receive a memorandum acknowledging receipt of the modification and explaining that the modification has not changed the original “Exempt from IRB Review” determination.
- The proposed modification does change the original “Exempt from IRB Review” determination. In this situation, the PI will receive a memorandum acknowledging receipt of the modification and explaining why the proposed modification has changed the original “Exempt from IRB Review” determination to another category. The memorandum will also inform the PI as to whether the proposed modifications have been approved via the expedited review procedures or will require full committee review.

4. **What to expect**

The IRB Chair will review modifications to studies initially categorized as Exempt from IRB Review or his/her designee via expedited review procedures. A PI can expect a response to his/her proposed modifications to a study exempt from IRB review within 2 – 3 weeks. However, please keep in mind that this turnaround timeframe is dependent on the responsiveness of the PI or his/her research team to OHR inquiries, if any. Once the IRB Chair or designee makes a determination regarding the proposed modification, the PI will receive a Modification Acknowledgement Letter. This letter will identify which of the 2 determinations outlined above have been made.

**B. Minor vs. Major Modification**

A **minor modification** is a change to a study that does not materially affect an assessment of the risks and benefits of the study, e.g., a change that is of minimal risk to the subject. Minor modifications include, but are not limited to, administrative changes to include change in telephone numbers, change in PI, research coordinator, etc; a reduction in an investigational drug dose or a reduction in amount of blood to be drawn, addition of, or changes, to recruitment materials/methods, and/or extending accrual period. Alternatively, a **major modification** is a change that materially affects an assessment of the risks and benefits of the study, e.g., changes increase risks to the subjects. Examples of major modifications include increase in dosing or amount of blood to be drawn, additional radiation exposure, extending the duration of the study, multiple changes in or complete change to study design, e.g., the addition of tissue banking requirements, and/or additional study populations, subjects.

1. **When to submit**
All proposed modifications to previously approved studies are processed and reviewed upon receipt of a complete proposed modification request, see below. Such requests are reviewed on a first come first serve basis. PIs must submit proposed modifications prior to implementing such changes unless the proposed change is necessary to eliminate immediate hazards to subjects.

**PIs submitting proposed major modifications to previously approved studies need to abide by the FCR submission deadlines because these deadlines apply to all actions requiring full committee review, e.g., major modifications. Alternatively, PIs submitting proposed minor modifications to previously approved studies need not abide by the FCR submission deadlines because proposed minor modifications are reviewed and approved by the IRB Chair or designee; not the full committee.**

2. **What to submit**

For **minor modifications** to previously approved research, the PI must submit 1 copy of a memorandum to the IRB Chair outlining the proposed modifications along with the following, as appropriate:

- If the modification affects the approved informed consent/assent/research subject authorization form - a copy of the original informed consent/assent/research subject authorization form with the requested modifications highlighted (now referred to as the modified informed consent/assent form) and a non-highlighted modified informed consent/assent/research subject authorization form with a new version date, and/or
- If the modification affects the approved protocol - a copy of the original protocol with the requested modifications highlighted (now referred to as the modified protocol) and a non-highlighted modified protocol with a new version date; and/or
- If the modification affects previously approved recruitment materials – the modified recruitment materials; and/or
- If the modification affects previously approved data gathering instruments – the modified surveys/questionnaires, etc.

For **major modifications** to previously approved research, the PI must submit 15 copies of a memorandum to the IRB Chair outlining the proposed modifications along with 15 copies of the information outlined above, as appropriate.

3. **How the submission is processed**

The OHR staff will review the proposed modification memorandum and attached documentation and make a preliminary determination as to whether the proposed modification qualifies as a minor or major modification. If it is determined that information is missing, the PI will be notified, via email, as to what information is still required. Once OHR makes a preliminary determination regarding the proposed modification, the IRB Chair or designee will review the preliminary determination. If the IRB Chair or designee determines that a proposed modification qualifies as a minor
modification, the modification will be reviewed via expedited review procedures. The IRB Chair or designee will be provided with a copy of all of the information outlined above, as appropriate.

Alternatively, if the IRB Chair or designee determines that a proposed modification qualifies as a major modification, an OHR staff member will inform the PI of this decision, either by a phone or by email. In this situation, an OHR employee will explain why a particular modification has been found to be major. The PI will be informed of what steps s/he must take in order to have his/her modification reviewed by the full GWU Medical IRB.

Major modifications, which require FCR, are assigned to one (primary) reviewer. The primary reviewer is provided with a copy of all the information outlined above, as appropriate. In addition, the primary reviewer is also provided with a copy of, or is given access to, the complete protocol including any modifications previously approved by the IRB. The primary reviewer may request additional information from the PI prior to the meeting at which the modification is to be reviewed. In addition, all other IRB members will be provided with the memorandum outlining the modification, a protocol summary, and a copy of all the information outlined above, as appropriate. At the scheduled meeting, the primary reviewer will present the major modification to the other IRB members. Following the presentation, other IRB members may add their comments/concerns regarding the modification. Following additional comments, if any, the full committee will bring the modification to a vote.

4. What to expect

A PI can expect a response to a proposed minor modification within 2 – 3 weeks. However, please keep in mind that this turnaround timeframe is dependent on the responsiveness of the PI or his/her research team to OHR inquiries, if any. Once the IRB Chair/Associate/Vice Chair approves a proposed minor modification, the PI will receive a “Modification Approval Letter – Expedited Review.” This letter will be accompanied by GWU IRB approved documents that have been changed as a result of the proposed minor modification.

Modifications requiring full committee review will be scheduled for the next upcoming IRB meeting. A PI can expect a response to his/her proposed major modifications within 4 – 6 weeks; depending on the timing of the submission of proposed modification, the next scheduled IRB meeting, and the diligence of the PI and his/her research team should revisions be requested. Once the IRB approves a proposed major modification, the PI will receive a “Modification Approval Letter – Full Committee Review.” This letter will be accompanied by GWU IRB approved documents that have been changed as a result of the proposed minor modification.

Please keep in mind that any proposed modifications to informed consent documents must take into account both prospective research subjects as well as research subjects already enrolled in the study, if applicable. The IRB Chair or designee makes the determination as
to whether already consented subjects need to be re-consented based on the GWU IRB guidance regarding when significant new findings developed during the course of research must be provided to enrolled subjects, which can be found in Chapter 4 of this Manual. If it is determined that such proposed modifications to the informed consent/assent forms require the re-consenting of already-consented subjects, such re-consenting can be addressed using an addendum to the initial informed consent document or by re-consenting the subject using the approved modified informed consent document. For instance, the PI may need to modify the approved informed consent form to include additional risks associated with the study. In this situation, the PI will have to inform already enrolled subjects of the change in risks associated with participation in the study.
CHAPTER 7: CRITERIA FOR IRB APPROVAL

Pursuant to federal regulations (45 CFR 46.111 and 21 CFR 56.111), the GWU Medical IRB may only approve research that satisfies all of the following requirements:

I. **Risks to Subjects Are Minimized**

This is ensured by PIs using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and are already being performed on the subjects for diagnostic or treatment purposes, when appropriate.

*Risks* to subjects are reasonable in relation to anticipated *benefits* to subjects, if any, (e.g., improved health for the research subjects) or society (e.g., knowledge to be gained from the research is considered important). In evaluating risks and benefits, the GWU Medical IRB only considers those risks/benefits that may result from the research as distinguished from risks/benefits of therapies the subjects would receive even if not participating in the research.

- **Risk** is defined as the probability of harm or injury (physical, psychological, social or economic) occurring as a result of participation in a research study. Both the probability and magnitude of possible harm may vary from minimal to significant. Please note that federal regulations only define minimal risk.

- **Benefit** is defined as a values or desired outcome; an advantage.

II. **Selection of Subjects is Equitable**

In making this assessment, the purposes of the research as well as the setting in which the research will be conducted must be taken into consideration. In making this assessment the GWU Medical IRB should also be particularly aware of the special problems associated with research involving vulnerable populations.

III. **Informed consent**

This is sought and appropriately documented from each subject or the subject’s LAR prior to the subject participating in the study in accordance with, and to the extent required by, federal regulations, district/state laws, and GWU Medical IRB policies. In making this assessment, the GWU Medical IRB reviews the proposed informed consent method as well as the actual informed consent document to ensure that subjects are adequately informed about the proposed research. Moreover, the IRB evaluates the proposed informed consent information in light of the risks and benefits of the proposed research procedures.

When appropriate, the research includes adequate provisions for monitoring the data collected to ensure the safety of the subjects. The GWU Medical IRB may determine that certain protocols require more than annual review and/or needs verification from other sources that no material changes have been made since the previous review.
IV. Subject Privacy and Confidentiality is Protected

The GWU Medical IRB must ensure that there are adequate provisions to protect the privacy of subjects and maintain confidentiality of the research data. These criteria warrant greater attention now with the enforcement date of the Health Insurance Portability and Accountability Act (HIPAA) privacy regulations. Please refer to Chapter 9 of this Manual for a more thorough discussion regarding what HIPAA considerations must be taken into account when reviewing a proposed research protocol involving protected health information.

Additional safeguards are included in the proposed research to protect the rights and welfare of subjects who are likely to be vulnerable to coercion or undue influence (e.g., vulnerable populations). Such vulnerable populations include, but are not limited to, children, prisoners, pregnant women, and fetuses.
CHAPTER 8: CONFIDENTIALITY AND PRIVACY ISSUES RELATING TO HUMAN SUBJECT RESEARCH

I. Confidentiality of Identifiable Information

In all human subject research, confidentiality of identifiable information is presumed and must be maintained unless the PI obtains the express permission of the subject to do otherwise. The general rule regarding confidentiality is the more sensitive the material gathered/assessed as a result of a human subject study, the greater the care that must be exercised to ensure that confidentiality is maintained. Ordinarily, the following requirements must be met:

- Questionnaires, inventories, interview schedules, and other data-gathering instruments and procedures should be carefully designed to limit the personal information to be acquired to that, which is essential;
- Data that could reveal a subject’s identity should be stored in files accessible only to the PI and authorized staff;
- As early as feasible, the data should be coded to remove identifying information;
- The identity of subjects must not be released except with their express permission;
- Use of existing data that were originally obtained for different purposes and that involve identifiable subject information, requires examination of the risk involved. There should be a determination of whether the new use is within the scope of the original consent or whether it is necessary or feasible to obtain additional consent; and
- Anonymity of the subjects must be preserved.

II. Direct and Indirect Identification of Subjects

A. Direct Identifiers of Subjects.

PIs should be aware that concerns regarding confidentiality involve the possibility of both direct and indirect identification of subjects through the information they provide. The types of data that can directly identify subjects include information such as their names, addresses, phone numbers, social security numbers, etc. As a general matter, a PI should consider direct identifiers as any information that should be stripped in order to make the information unidentifiable.

B. Indirect Identifiers of Subjects

In cases where research focuses on a narrowly defined universe of subjects or where categorizing information can be used to reduce the universe of subjects, identification of some subjects may be possible through the use of one or two indirect identifiers. For instance, if researchers collect information from a single small town or a single school, a few pieces of information such as the subject’s gender, ethnicity, income or occupation might be sufficient to uniquely identify a subject. Procedures that can be taken to minimize the chances of indirect identification include:

- Not releasing individual data and only reporting data in aggregate form; and/or
- In cases where data cannot be aggregated (such as in a qualitative analysis) or must be reported or made available in individual form (a requirement of some journals and
professional associations), changing, grouping or removing information that could indirectly identify subjects.

C. Confidentiality vs. Use of Audio and Videotaping of Research Subjects

Some research protocols use audio and videotaping of research subjects. Whenever such taping is to occur, the subject should be informed of this via the informed consent process. Moreover, explicit consent must be obtained for any public use of the tapes such as use in the classroom or as part of a public presentation of the research results because this constitutes a waiver of the normal confidentiality of research data. Such explicit consent can be obtained via a study specific Audio/Video Research Form. This sample Audio/Video Research Form is available at http://www.gwumc.edu/research/forms.htm.

III. Certificates of Confidentiality

Some proposed human subject research studies involve the collection of data on sensitive matters such as sexual behavior or criminal activities. Under federal law, researchers can obtain from the National Institutes of Health (NIH) an advance grant of confidentiality that will protect the research staff from being prosecuted for withholding subpoenaed information regarding sensitive research data. This advance grant of confidentiality is called a Certificate of Confidentiality (COC). A COC protects information that is subpoenaed by any civil, criminal, administrative, or legislative body, whether at the federal, state, or local level. In order for a COC to be effective, the PI must request a grant of confidentiality from an appropriate NIH official. For additional COC information, including application and submission instructions and frequently asked questions, go to the NIH Certificates of Confidentiality Kiosk, online at http://grants1.nih.gov/grants/policy/coc/index.htm.

COC protection is available for all “sensitive research” regardless of funding source. Sensitive research is defined as involving the collection of information falling into any of the following categories:

(a) Information relating to sexual attitudes, preferences, or practices;
(b) Information relating to the use of alcohol, drugs, or other addictive products;
(c) Information pertaining to illegal conduct;
(d) Information that if released could reasonably be damaging to an individual's financial standing, employability, or reputation within the community;
(e) Information that would normally be recorded in a patient's medical record, and the disclosure of which could reasonably lead to social stigmatization or discrimination; and
(f) Information pertaining to an individual's psychological well-being or mental health.

Information in other categories, not listed above, might also be considered sensitive because of specific cultural or other factors, and protection can be granted in such cases upon appropriate justification and explanation.
Please note that when a COC is sought and approved for a particular study, the informed consent form must disclose the use of the COC. Moreover, please note that all proposed COCs must be approved by the AVP for OHRCTT.

IV. Privacy and HIPAA

Please refer to Chapter 9 entitled for guidance regarding human subject research protocols involving protected health information (PHI), limited data set information (LDS) and/or de-identified health information.
CHAPTER 9: HIPAA AND ITS IMPACT ON HUMAN SUBJECT RESEARCH

The Health Insurance Portability and Accountability Act of 1996 (HIPAA) and one of its implementing regulations, the Privacy Rule, establish the conditions under which protected health information (PHI) may be used or disclosed by a covered entity for research purposes. Where research is concerned, the Privacy Rule protects the privacy of individually identifiable health information created or received by a covered entity, while at the same time, ensuring that researchers continue to have access to medical information necessary to conduct vital research.

Since the implementation of HIPAA, HHS offices/institutes have issued various publications explaining how the HIPAA Privacy Rule impacts specific research activities. To date, none of the publications have been issued in the Federal Register; thus, GWU considers these publications unofficial guidance only. These publications and their associated links are provided below:

2. Health Services Research and the HIPAA Privacy Rule (not yet provided);

You may notice that some guidance provided in the publications may be in conflict with GWU IRB policy. In the event you notice such a discrepancy and would like to discuss the discrepancy, please contact OHR.

Note: Protocols involving non-PHI need not be reviewed under the HIPAA Privacy Rule; however, such studies must be reviewed under the Common Rule (45 CFR Part 46) and/or the Food and Drug Administration (FDA) human subjects protection regulations (21 CFR Parts 50 and 56). Whenever a researcher is not sure whether a proposed study involves the use or disclosure of PHI, the researcher can complete the HIPAA Sample Worksheet for Determining the Type of Data Being Used or Disclosed, available at http://www.gwumc.edu/research/forms.htm. This worksheet will assist the researcher in making a preliminary decision regarding whether HIPAA applies to his/her protocol.

I. Use and/or Disclosure of PHI for Research Purposes

HIPAA defines PHI, the type of health information governed by HIPAA, as individually identifiable health information (IIHI) that has been created or received by a covered entity (CE). IIHI is health information and associated demographic (identifying) information that either: identifies an individual (“identified” information) or could reasonably be used to identify an individual (“identifiable” information). Health information that has no direct identifiers, but includes a unique code-link is “identifiable,” as described below. Alternatively, health
information that has no direct identifiers, but includes a code-link that is not derived from or related to information about an individual and cannot be translated to identify the individual is not “identifiable” as described below.

**Coded:** Data or biological specimens that are linked to a specific individual by a **code-link** derived from or related to information about the individual (e.g., encrypted social security number, subject initials\(^7\), medical record number, etc.) rather than a direct identifier (e.g., name or SSN). Such a “code-link” directly or indirectly links the data or specimen to a specific individual. This type of code-linked data is “identifiable.”

**Unlinked:** Data or biological specimens that may have been collected with identifiers, but all identifiers and code-links derived from or related to information about the individual have been removed or destroyed. Such unlinked data or biological specimens may include a code or other means of record re-identification, provided that the code is not derived from or related to information about the individual and can not be translated to identify the individual (e.g., a random number code) and the CE does not use or disclose the code for other purposes or disclose the mechanisms for re-identification. In such situations, it would be extremely difficult for a specific individual to be identified on the basis of such unlinked data. This type of unlinked data is not “identifiable.”

HIPAA defines a **covered entity (CE)** as a health plan, health care clearinghouse, or a health care provider if the health care provider 1) provides health care, 2) is paid for providing health care, and 3) the provider’s payment for health care involves the electronic transmission of health information. Please note that the (3) qualifiers noted above apply only to health care providers; they do not apply to health care clearinghouses or health plans. This is why only certain health care providers are covered entities (e.g., health care providers who electronically transmit health information for payment of rendered health care services) while all health plans and health care clearinghouses, regardless of whether they electronically transmit health information, are covered entities.

Individual researchers are not themselves considered CEs, unless they also provide/render health care services and electronically transmit health information for payment of such services. If, however, researchers are employees or other workforce members of a CE, e.g., MFA employee, they become a CE. At GWU, the MFA and the George Washington University Hospital (GWUH) are separate institutional covered entities. Thus, the entire workforce of the MFA and GWUH, including MFA and/or GWUH researchers who do not directly render healthcare services, are considered separate CEs. Alternatively, at GWU, the University, as an institution is not a covered entity. Please note, however, that some individual University faculty members are considered health care providers under the HIPAA definition of a covered entity. All University researchers are responsible for determining whether s/he is an individual covered entity. University faculty with questions regarding covered entity status as it relates to human subject research should consult with the Office of Research Compliance.

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\(^7\) Pursuant to an NIH publication entitled Research Repositories, Databases, and the HIPAA PRIVACY RULE individuals’ initials are considered to be identifiers because they are derived from the individual’s name. Thus, for information to be “not-identifiable” an individual’s initials must be stripped from the information.
A. Use vs. Disclosure of PHI

HIPAA regulates the use and disclosure of PHI for research. Any use or disclosure of PHI for a research purpose requires obtaining some form of HIPAA-required permission, as outlined below.

As illustrated in Figure 1, “use” of PHI means use within the covered entity. For example, use (review, analysis, recording, collecting) of MFA’s PHI by any member of MFA’s workforce is a “use.” The same applies to GWUH. For an individual covered entity, “use” is limited to that individual.

“Disclosure” of PHI means sharing (give, transmit or allow on-site access to) the PHI with a person or entity outside of the covered entity (see Figure 1). For example, sharing MFA maintained PHI with any researcher (investigator, sponsor, CRO, etc.) who is not a member of the MFA workforce is a “disclosure,” even if that researcher is part of GWU and even if the PHI is reviewed on-site at the MFA.

Figure 1

To help distinguish between a use and a disclosure of PHI, this Manual uses the terms inside and outside researchers to refer to researchers who are part of the covered entity or outside the covered entity, respectively. Thus, the term inside researcher is defined as a member of the workforce of the covered entity that maintains the PHI; whereas the term outside researcher is defined as a researcher who is not a member of the workforce of the covered entity that maintains the PHI. An outside researcher may be an investigator or a representative of a sponsor, contract research organization (CRO) or subject recruitment service.

To illustrate how these definitions apply at GWU, with regard to MFA medical records:

- A MFA researcher is an ‘inside’ researcher;
- An UHS researcher is an ‘outside’ researcher;
- A GWU (MC) faculty member is an ‘outside’ researcher;
- A faculty member of another university is an ‘outside’ researcher;
- A representative of the sponsor, CRO or recruitment service is an ‘outside’ researcher.

B. Criteria for Use or Disclosure of PHI for Research Purposes
Pursuant to HIPAA, a covered entity may use (receive, access, review, create, record, transmit, store) within a particular GWU research team and/or disclose outside of a GWU research team PHI in the course of conducting research with either:

An individual research subject authorization that satisfies the requirements of 45 CFR 164.508; (See Section II below) or

Without an individual research subject authorization (RSA) under one of the following circumstances:

a. When a Researcher Obtains GWU IRB Approval for Waiver or Alteration of a Research Subject Authorization for the Entire Study; (See Section IIIA below);

b. When a Researcher Obtains GWU IRB Approval for Partial Waiver of RSA for Recruitment Purposes (coupled with a RSA) (See Section IIIB below);

c. When a Researcher Obtains Approval from a Covered Entity to Use or Disclose PHI for Reviews Preparatory to Research (RPR) Purposes (See Section IIIC below);

d. When a Researcher Obtains Approval from a Covered Entity to Use or Disclose PHI Relating to Decedents (see Section IIID below);

e. When the Researcher Obtains GWU IRB Approval for the Use or Disclosure of Limited Data Set Information (LDS) (coupled with a Data Use Agreement) (See section IIIE below); or

f. When the Researcher Obtains GWU IRB Approval for the Use or Disclosure of De-Identified Information. (See section IIIF below).

C. Requirements for Use and/or Disclosure of PHI for Research Purposes

1. Minimum Necessary Use/Disclosure of PHI

A CE may use or disclose only the minimum PHI reasonably necessary for the intended purpose. In research, the uses/disclosures of PHI must be the minimum necessary to accomplish the objectives stated in the protocol. The single exception to this limitation is that the minimum necessary rule does not apply to uses/disclosures of PHI when a subject explicitly gives permission for the use/disclosure in a research subject authorization form (see below).

2. Tracking disclosures of PHI

Disclosures of PHI by a CE to ‘outside’ researchers are subject to HIPAA’s accounting requirement and must be tracked by the CE. The accounting requirement is explained below. Briefly, a CE is required to track and maintain records for six years disclosures of PHI pursuant to Reviews Preparatory to Research Requests, Decedent PHI Requests, Waivers of Research Subject Authorizations, Partial Waivers of Authorizations for Recruitment Purposes, and Business Associated Agreements. *Disclosures made to ‘outside’ researchers pursuant to a research subject authorization do not need to be
Moreover, disclosures of limited data set or de-identified information to outside researchers do not need to be tracked.

Figure 2 below illustrates the HIPAA requirements that apply to “uses” of PHI by ‘inside’ researchers and “disclosures” of PHI to ‘outside’ researchers.

**Figure 2**

<table>
<thead>
<tr>
<th>Mechanisms for Use or Disclosure of Health Information</th>
<th>Minimum Necessary</th>
<th>Tracking of Disclosures</th>
</tr>
</thead>
<tbody>
<tr>
<td>Research Subject Authorization (RSA)</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Waiver of RSA</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>Partial Waiver of RSA for Recruitment Purposes</td>
<td>YES</td>
<td>YES</td>
</tr>
<tr>
<td>RPR</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Decedent PHI</td>
<td>YES</td>
<td></td>
</tr>
<tr>
<td>Limited Data Set Information (with DUA)</td>
<td>YES</td>
<td>NO</td>
</tr>
<tr>
<td>De-Identified Information</td>
<td>NO</td>
<td>NO</td>
</tr>
<tr>
<td>Business Associates</td>
<td>YES</td>
<td>YES</td>
</tr>
</tbody>
</table>

II. **Research Use/Disclosure With Individual Research Subject Authorization**

The Privacy Rule permits a covered entity to use or disclose PHI for research purposes when a research participant authorizes the use or disclosure of information about him or herself. This research participant authorization is called a Research Subject Authorization (RSA). A RSA will typically be sought for most clinical trials and some records research. A sample RSAF is available at the GWU Office of Human Research website at [http://www.gwumc.edu/research/forms.htm](http://www.gwumc.edu/research/forms.htm).

The Privacy Rule allows for a RSA to be combined with an ICF (or with any other legal permission related to the research study). At GWU, the RSA is separate from the traditional informed consent document used in research. GWU has decided not to combine such documents because each document is intended for a different purpose i.e., the ICF is intended to protect the safety and well being of the subjects whereas the RSA is intended to protect the privacy of the subject’s health information collected as part of the research study. Thus, it is believed that keeping these documents separate will help maintain the distinction between the two documents.
Under HIPAA, a RSA must contain core elements and required statements that are study specific. The RSA gives the GWU research team (as described in the GWU IRB Submission Form and the ICF) the authority to use, create, and disclose health information about a particular subject as part of a specific research study. For example, if the covered entity/researcher intends to seek reimbursement from the research subject's health plan for the routine costs of care associated with the protocol, the authorization must describe types of information that will be provided to the health plan.

It is extremely important that all uses of PHI and all persons/entities that will use or receive PHI under a given study be listed in the RSA because if such uses/persons/entities are not listed, the PHI cannot be used for the purpose or disclosed to the persons/entities. Rather, a new RSA will be required before a GWU research team member could use the PHI as initially intended and/or disclose the PHI to a previously overlooked person/entity.

A. Enrollment of subjects after April 14, 2003

As a general rule, all human subjects who enroll in a research study on or after April 14, 2003 (i.e., sign an informed consent form or are re-consented), which involves the use or disclosure of PHI, must sign a RESEARCH SUBJECT AUTHORIZATION FORM that has been approved by the GWU IRB. A sample RSAF is available at the GWU Office of Human Research website at http://www.gwumc.edu/research/forms.htm.

In some limited situations, the GWU IRB may approve a waiver of research subject authorization (see Section III below) for research involving participation of live human subjects.

B. On-going studies that started prior to the implementation of HIPAA

1. Research subjects enrolled prior to April 14, 2003

Subjects that were enrolled in GWU IRB approved studies prior to April 14, 2003, which involve the use or disclosure of PHI, do not need to sign a Research Subject Authorization Form. Under HIPAA, a RSA is not needed for such subjects as long as the subjects were enrolled in the study with an IRB-approved informed consent form or waiver of consent. These types of studies are considered grandfathered under HIPAA.

2. Protocol Amendments

If the research protocol of an on-going study involving the use or disclosure of PHI is amended after April 14, 2003 such that previously enrolled subjects need to be re-consented, the subject must also sign a RESEARCH SUBJECT AUTHORIZATION FORM.

III. Research Use/Disclosure Without Research Subject Authorization

What follows is a description of the six circumstances under which a GWU researcher may use/disclose PHI in the course of conducting research without an individual RSA. The last two circumstances address the use/disclosure of limited data set information (a subset of PHI) and de-
identified health information (PHI that has been de-identified to the extent that it is no longer covered by HIPAA) for research purposes.

A. IRB Approval of a Request to Waive/Alter Research Subject Authorization for Entire Study

Under HIPAA, research that involves no more than minimal risk to subjects’ privacy may be conducted without a RSA, or with an alteration to the authorization’s requirements, if the IRB prospectively approves a waiver of RSA. Examples of research that might qualify for a waiver of research subject authorization include:

- Epidemiological research involving large numbers of medical records and/or clinical databases;
- Records-based research that requires access to multiple existing patient records;
- Telephone interviews;
- Research on decedents;
- When researchers are unable to use de-identified information and it is not practicable to obtain research participants’ authorization; or
- Utilization review research that may require the accession of thousands of billing records.

Under the Common Rule, a waiver or alteration of informed consent may be approved by the IRB if the research involves no more than minimal risk to the subjects. Because of the similar standards, as a general rule, in order for a study to qualify for a waiver of RSA the study must also qualify for a waiver of informed consent. Thus, to qualify for a HIPAA waiver of authorization, the research must meet all of the following criteria:

1. Criteria for Waiver of Research Subject Authorization

   a. The use/disclosure of PHI involves no more than minimal risk to the privacy of the subjects because there is:

      - An adequate plan to protect the identifiers from improper use and disclosure;
      - An adequate plan to destroy the identifiers at the earliest opportunity; and
      - An adequate written assurance that PHI will not be reused or disclosed except as permitted under HIPAA. If PHI will be disclosed to persons outside the GWU Research Team, the PI must submit a copy of the assurance to the IRB. The assurance may be in the form of a research agreement, data use agreement, business associate agreement or material transfer agreement. If no such agreement exists, a letter from the recipient of the PHI to the GWU researcher will suffice.

   b. The research could not practicably be conducted without the waiver or alteration.

In practical terms, this means that a waiver of authorization will not be approved for research involving interaction with live subjects (because it is possible for the investigator
to obtain an authorization from subjects). Requests for waivers are appropriate for studies of existing data (e.g., medical records or databases) or biological specimens (e.g., private or publicly maintained tissue repositories) and when access to subjects is not feasible. Alteration of the required elements for an authorization may be appropriate for research involving interaction with live subjects and highly sensitive information (e.g., HIV/AIDS, domestic abuse, drug use) for which subjects may not want to sign the authorization form.

c. The research could not practicably be conducted without PHI.

To meet this criterion, the PI must explain to the IRB why either de-identified data or a limited data set information (LDS) (defined below) is not sufficient to achieve the study’s research objectives.

2. Criteria for Waiver of Informed Consent

a. The research involves no more than minimal risk to the subjects;
b. The waiver will not adversely affect the rights and welfare of the subjects;
c. The research could not practicably be carried out without the waiver or alteration; and
d. When appropriate, subjects will be provided with additional pertinent information after participation.

Please note that some studies that are exempt from IRB review under the Common Rule, including the requirement for obtaining informed consent or waiver thereof, will not be under HIPAA. This discrepancy results from the fact that HIPAA protects the privacy of information whereas the Common Rule protects the safety and wellbeing of the subjects. Thus, studies involving demonstration projects that are exempt from IRB review and informed consent requirements will nevertheless require an IRB-approved waiver of research subject authorization if such studies involve PHI. In those situations, the researcher would only need to submit a Waiver of Research Subject Authorization Form.

To request a waiver or alteration of research subject authorization, a researcher must submit the following to the GWU IRB:

- **WAIVER OF RESEARCH SUBJECT AUTHORIZATION REQUEST FORM**, signed by Privacy Officer of the covered entity that maintains the PHI, available at: [http://www.gwumc.edu/research/forms.htm](http://www.gwumc.edu/research/forms.htm). The covered entity that maintains the PHI must disclose only the minimum necessary to conduct the research and must track the disclosures.
- Waiver/Alteration of Informed Consent Request Form; **and**
- IRB Submission Form and related materials.

Usually, the GWU IRB will be able to conduct an expedited review of a request for a waiver of authorization. If the IRB approves the waiver of authorization, an approval memo signed by the IRB chair or designee will be sent to the researcher. If the criteria for waiver of authorization are not met or, if there is any other reason that the waiver may not
be granted, a memo signed by the IRB chair or designee will be forwarded to the researcher explaining the reason(s) for the disapproval.

Please note that a waiver of authorization also may be approved by the GWU IRB for PHI to be used or disclosed for the exclusive purpose of recruiting subjects. This is called a “partial” waiver of research subject authorization and is explained in the next section.

B. IRB Approval of a Request for Partial Waiver of RSA For Recruitment Purposes

Pursuant to HIPAA, a partial waiver of authorization may be requested from the GWU IRB when a researcher wishes to use PHI for the exclusive purpose of recruiting subjects. The criteria for a ‘partial’ waiver are the same as those listed above under waivers of authorization for the study itself. It is called a “partial” waiver of research authorization because the waiver covers the use or disclosure of PHI for recruitment only, but not for the research itself (e.g. the research activities conducted following subject enrollment). An example of this would be when a researcher wants to use information in MFA medical records to send a recruitment letter to prospective subjects.

Studies involving interaction with live subjects typically will not qualify for a waiver of research authorization for the entire study, but a partial waiver of authorization may be requested to use PHI just to recruit subjects. In that situation, the Principal Investigator submits a research protocol to the GWU IRB requesting 1) a partial waiver of research subject authorization to obtain PHI from a covered entity for subject recruitment, and 2) a Research Subject Authorization to use and disclose PHI in the research study once subjects are enrolled.

To comply with the ‘minimal risk’ requirement that applies to all uses and disclosures of PHI without an RSA, researchers who obtain PHI to contact prospective subjects must destroy the identifiers from the PHI of persons who are not enrolled in the study when the candidate is rejected as a subject or enrollment is closed, whichever occurs first.

To request a partial waiver of authorization to use another covered entity’s PHI for subject recruitment, a researcher must submit the following to the GWU IRB:

- A PARTIAL WAIVER OF RESEARCH SUBJECT AUTHORIZATION REQUEST FORM, signed by the Privacy Officer of the covered entity that maintains the PHI, available at: http://www.gwumc.edu/research/forms.htm. The covered entity that maintains the PHI must disclose only the minimum necessary to recruit subjects and must track the disclosures;
- A RESEARCH SUBJECT AUTHORIZATION form to use/disclose PHI for the research study; and
- An IRB SUBMISSION FORM AND RELATED MATERIALS (e.g., recruitment letter, script of telephone communications, script of in-person interviews, etc.).

The HIPAA requirements that apply to subject recruitment depend on whether PHI will be involved in the recruitment process. PHI may be involved in two ways: 1) existing PHI (e.g. in medical records, databases or tissue repositories) maybe used to identify and directly contact prospective subjects (targeted contacts); and 2) new PHI may be collected when respondents to recruitment ads (non-targeted contacts) are screened in follow-up interviews.
Please note that non-CE researchers may use existing IIHI in their possession or obtained from other non-CE sources for subject recruitment without triggering any HIPAA requirements (no PHI is involved). For example, non-CE researchers may maintain their own research databases or may use public health databases to identify and contact subjects.

1. **Subject Recruitment Options and the Effect of HIPAA on Such Options**

In order to provide you with a better understanding of the subject recruitment options available at GWU and how these options are affected by HIPAA, below is a list of recruitment options and what effect HIPAA will have on those options, if any. The first 2 options deal with GWU CE-researchers, whereas the last 2 options deal with GWU Non-CE researchers.

a. **CE-Researchers Using Targeted Contacts**

A GWU CE-researcher may speak directly with his/her patients who may qualify for and be interested in a particular research protocol. The GWU CE-researcher does not have to be involved in the particular research protocol that is discussed with the patient. This is a permitted disclosure under HIPAA; thus, a partial waiver of authorization is NOT required. Alternatively, if someone other than a patient’s treating provider wishes to use PHI to contact a prospective research subject, the researcher must first obtain approval of a **partial waiver** of research subject authorization by the GWU IRB. In this scenario, the person contacting the prospective subjects could be the patient’s treating provider (preferred method), a member of the research team (covered entity or non-covered entity), a subject recruitment service or a representative of the sponsor or contract research organization (CRO) (less preferred method).

Prospective subjects may be contacted directly by **personal contact, mail, email or telephone**. PHI that might be used for recruitment purposes include patient/surgical lists, medical records, recruitment databases or tissue repositories. As described below, targeted contacts may be made by the individual’s treating provider or by another researcher obtaining PHI from a CE.

Under either of the scenarios above, the researcher may use either existing or not yet compiled PHI to directly contact prospective subjects. The GWU covered entity holding the PHI may use or disclose only the minimum PHI necessary to contact the subjects. When a GWU covered entity **discloses** PHI to an outside researcher for subject recruitment under a partial waiver, the covered entity must track the disclosures. The researcher who receives the PHI must destroy the identifiers of individuals who are not enrolled in the study either when they are not enrolled (the individual declines or is rejected) or enrollment is closed, whichever occurs first.

b. **CE-Researchers Using Non-targeted contacts**

i. Initial recruitment ad
Non-targeted contacts include newspaper ads, TV or radio ads, the Internet, bulletin boards, etc. providing information about the study and the contact information of a person/entity for the prospective subject to contact if interested in participating. In this situation, PHI is not used to make the initial contact, but PHI may be collected during the follow-up response to a non-targeted contact, as explained below.

ii. Follow-up contact with respondents

Non-targeted ads typically instruct persons who may be interested in participating in a study to call or email someone associated with the study at the number or address provided on the ad, which has already been approved by the GWU IRB. Follow-up contact with respondents by researchers may involve the collection of PHI in either of the following scenarios:

- The person communicating with respondents is a CE (or part of the CE’s workforce, e.g., the Study Coordinator) and the person obtains IIHI from respondents as part of the screening process (step 2 in diagram, below). IIHI that is created or received by a CE becomes PHI.

- The person communicating with respondents is not a CE, the person obtains IIHI from respondents as part of the screening process (step 2 in the diagram, below) and the person forwards the IIHI to a researcher who is a CE (step 3 in the diagram, below). Once IIHI is forwarded to the CE, it becomes PHI.

This scenario is common when a CRO or subject recruitment company conducts the initial screening of respondents and then forwards information (IIHI) from candidate subjects to the PI. If the research team includes PIs who are a CE, the information obtained during recruitment becomes PHI.
c. Recruitment by CE Researchers

The following examples illustrate the HIPAA requirements for subject recruitment involving follow-up responses to non-targeted ads by GWU CE-researchers:

- A GWU CE-researcher may publish an IRB-approved advertisement for a research study instructing potential subjects to call a member of the GWU research team. If any PHI will be collected during the conversation, the GWU Principal Investigator must first obtain GWU-IRB approval of a partial waiver of research subject authorization. PHI of subjects who are not enrolled in the study must be destroyed when the candidate is rejected as a subject or enrollment is closed, whichever occurs first. Also, the PHI collected during the conversation must be the minimum necessary to recruit subjects for the specific research protocol. This means that questions asked during the telephone screening must be limited to those related to the inclusion/exclusion criteria of a specified protocol. The GWU IRB will review the script of the telephone conversation to ensure that the script is limited to only those questions relative to the inclusion/exclusion criteria.

- A GWU CE-researcher may publish an IRB-approved advertisement for a research study instructing potential subjects to call a research subject screening service. According to HIPAA, if any IIHI will be collected during the conversation with the screening service, the GWU Principal Investigator must first obtain GWU-IRB approval of a partial waiver of research subject authorization prior to receiving the IIHI from the screening service because once the IIHI is provided to the GWU CE-researcher, the information becomes PHI. (IIHI + CE = PHI).

The service must destroy the identifiers of persons who do not meet the inclusion/exclusion criteria immediately. The service must destroy the identifiers of persons who do meet the inclusion/exclusion criteria once the information is forwarded to the Principal Investigator. The Principal Investigator must destroy the identifiers of PHI from persons who are not enrolled in the study when the candidate is rejected as a subject or enrollment is closed, whichever occurs first.
The PHI collected during the conversation must be the minimum necessary to recruit subjects for the specific research protocol. This means that questions asked during the telephone screening must be limited to those related to the inclusion/exclusion criteria of a specified protocol.

In addition, a Business Associate’s Agreement (see Section VII below) may be necessary if the service is conducting the recruitment on behalf of (is paid by) the covered entity.

d. Recruitment by Non-CE Researchers

The following examples illustrate the HIPAA requirements for subject recruitment involving follow-up responses to non-targeted ads by non-GWU researchers:

- A non-CE researcher may publish an IRB-approved advertisement for a research study instructing potential subjects to call a member of the GWU research team. IIHI may be collected from respondents in follow-up screening without triggering any HIPAA requirement providing no member of the GWU research team is a covered entity.
- A non-CE researcher may publish an IRB-approved advertisement for a research study instructing potential subjects to contact a co-investigator who is a covered entity. If the CE-co-investigator collects IIHI from respondents in follow-up screenings, the GWU IRB must approve a partial waiver of research authorization prior to placing the recruitment ad. The recruitment ad also must be reviewed and approved by the GWU IRB.

C. Approval from a Covered Entity to Use or Disclose PHI for RPR Purposes

Under the HIPAA RPR provision, a covered entity is permitted to allow on-site review of existing PHI by either ‘inside’ researchers or ‘outside’ researchers to screen subjects and/or develop a research protocol. These activities are part of “research” rather than treatment, but are considered ‘preparatory’ to the initiation of a research study. Thus, these RPR activities are not subject to review and approval by the GWU IRB. For the purpose of this Manual, subject screening does not involve contacting prospective subjects. Subject recruitment, which is discussed above, involves contacting prospective subjects.

Researchers often screen subjects for a particular research study by accessing already existing medical information maintained by a covered entity. Subject screening may involve reviewing medical records, a database or a tissue repository to determine the approximate number of potential subjects that might be available from a pool of patients or the clinical profile of prospective subjects. As stated above, the RPR provision is available to both inside and outside researchers to screen subjects. Please note that if an outside researcher reviews a GWU covered entity’s PHI, the outside researcher must do so on-site and may not remove the accessed PHI from the covered entity’s site.

Under HIPAA, the use of PHI under the RPR provision is limited as follows:
• The PHI may not be removed from the covered entity’s site;
• The PHI may be used only to prepare a research protocol or other similar preparatory research proposal; and
• The PHI must be necessary for the research purpose.

When making an RPR request to a covered entity the researcher must keep in mind that the PHI being accessed for RPR purposes must be the minimum amount of PHI necessary for the specific RPR purpose. Thus, if a researcher asks for more than the minimum necessary information required for a preparatory purpose, the researcher’s request should be denied by the covered entity.

To access a GWU covered entity’s PHI under an RPR review a researcher (‘inside’ or ‘outside’) must do the following:

• Complete and sign the GWU REVIEW PREPARATORY TO RESEARCH REQUEST FORM, available at: http://www.gwumc.edu/research/forms.htm;
• Have the covered entity’s Privacy Officer sign the completed form; and
• Maintain a copy of the signed form in the researcher’s file. The GWU IRB may request a copy of this form either as part of its review of a research protocol or a research compliance audit.

As stated above, RPR activities are considered ‘preparatory’ to the initiation of a research study and as a result are not subject to review and approval by the GWU IRB. However, please keep in mind that once a researcher decides to use the PHI that he/she accessed under a RPR activity to recruit potential subjects, such recruitment cannot occur until the GWU IRB has reviewed and approved the proposed recruitment plan. Unlike RPR activities, recruitment activities are considered part of the informed consent process and are regulated as “research.” Thus, researchers must obtain IRB approval of proposed recruitment activities, including the proposal to contact potential subjects using the PHI that was accessed under an RPR activity, prior to initiating any recruitment activities.

D. Approval by a Privacy Officer/ of a Covered Entity Maintaining Decedent PHI

Under HIPAA, a researcher may use or disclose PHI on deceased persons that is maintained by a covered entity if the researcher does the following:

• Complete the GWU DECEDENT PROTECTED HEALTH INFORMATION REQUEST FORM, available at: http://www.gwumc.edu/research/forms.htm;
• Has the covered entity’s Privacy Officer sign the completed form.
• Maintain a copy of the signed form for the researcher’s file; and
• Upon request, provide the covered entity with documentation of the subject’s death.

E. Approval for the Use/Disclosure of LDS Information

1. What is LDS?
HIPAA defines LDS as a limited set of PHI that may be used for research, but not subject recruitment. The advantage to using LDS for research is that a RSA is not required. Instead, a Data Use Agreement (DUA) is required between GWU and the recipient of the LDS. DUA requirements are explained more fully below.

Existing PHI may be used to create LDS by removing the following 15 direct identifiers of a research subject or of relatives, employers or household members of the research subject:

1. Names (initials do not have to be removed);
2. Telephone numbers;
3. Fax numbers;
4. Electronic mail addresses;
5. Social security numbers;
6. Medical record numbers;
7. Health plan beneficiary numbers;
8. Account numbers;
9. Certificate/license numbers;
10. Vehicle identifiers and serial numbers, including license plate numbers;
11. Device identifiers and serial numbers;
12. Web Universal Resource Locators (URLs);
13. Internet Protocol (IP) address numbers;
14. Biometric identifiers, including finger and voice prints; and
15. Full face photographic images and any comparable images.

LDS may include the following identifiers of a research subject or of relatives, employers or household members of the subject:

1. Any date;
2. Addresses, including town, city, state and five-digit zip code but not the street address; and
3. A unique identifying number, characteristic, or code-link.

2. Contents of a DUA

According to HIPAA, a DUA must:

i. Establish the permitted uses and disclosures of the LDS by the recipient of the LDS, consistent with the purpose of the research;
ii. Limit who can use or receive the data; and
iii. Provide that the recipient will:

- Not use or further disclose the information other than as permitted by the DUA or as otherwise required by law;
• Use appropriate physical, technical and administrative safeguards to prevent use or disclosure of the LDS other than as provided for in the DUA;
• Report to GWU any use or disclosure of the information not provided for by the DUA of which the recipient becomes aware;
• Ensure that any subcontractor to whom it provides the LDS agrees to the same restrictions and conditions that apply to the LDS recipient with respect to such information;
• Not identify the information or contact the individuals; and
• Not use or further disclose the information in a manner that would violate HIPAA’s requirements.

GWU covered entities must use the GWU template DUA to disclose LDS to a researcher. To access the DUA template, contact OHRCTT, 712 Ross Hall. The template DUA must be completed in accordance with the research protocol and signed by the GWU covered entity that is the source of the LDS. The GWU Office of Health Research Compliance, and Technology Transfer (see below) must execute all DUAs.

3. Use of GWU PHI to create LDS for research

A GWU covered entity may use its PHI to create LDS to disclose to a researcher only if

i. The researcher obtains approval from the GWU IRB for a waiver of research subject authorization for the GWU covered entity to use the PHI to create the LDS, if applicable;
ii. GWU covered entity completes and signs the GWU template DUA in accordance with the research protocol under IRB review;
iii. The recipient of the LDS signs the DUA;
iv. The Principal Investigator forwards the signed DUA to the Office of Health Research Compliance, and Technology Transfer (OHRCTT), located in Ross Hall, Room 712, for GWU signature and execution; and
v. Once signed, OHRCTT will provide Principal Investigator and the GWU covered entity with a copy of the executed DUA.

4. Receipt of LDS by a GWU researcher from a Non-GWU Source

GWU researchers who wish to obtain LDS from a non-GWU covered entity data source need to have a DUA executed between GWU (the institution, not the individual) and the source of the LDS. Please be advised that a GWU researcher requesting access to LDS maintained by a non-GWU source (e.g., Washington Hospital Center) will be asked to follow the source’s institutional policies and procedures for granting access to LDS. Thus, GWU researchers seeking LDS should ask for information about the source’s LDS policies/procedures to ensure compliance with HIPAA and timely compliance with all institutional requirements.
GWU researchers who use LDS from a non-GWU source must submit a copy of the DUA signed by the appropriate official at the non-GWU source along with their GWU IRB Submission form. GWU principal investigators of studies involving LDS should begin the DUA process at the same time the principal investigator initiates the IRB review process.

5. Disclosure of PHI by a GWU CE to ‘outside’ researchers to create LDS

A GWU covered entity may disclose PHI to an ‘outside’ researcher for the purpose of converting the PHI to LDS without a Research Subject Authorization. Disclosure of PHI for this purpose creates a business associate relationship and requires a Business Associate Agreement between GWU and the recipient of the PHI. Business Associate Agreements are described in Section VII, below. A Data Use Agreement may also be required, as follows, depending on who will use the LDS:

a. If the Business Associate intends to use the LDS (regardless of whether the GWU researcher also will use the LDS), a Data Use Agreement is required.

b. If the Business Associate creates the LDS for use or disclosure by the GWU researcher only (the Business Associate will not use the LDS), a Data Use Agreement is not required.

F. Approval of the Use or Disclosure of De-Identified Information

A covered entity (e.g., CE-researcher) may always use or disclose for research purposes health information, which has been de-identified (in accordance with §§ 164.502(d), 164.514(a)-(c) of the rule) without regard to the provisions outlined above.

Pursuant to HIPAA, one way that PHI can be de-identified is by removing 18 identifiers that are specified in the Privacy Rule. To de-identify data, researchers must:

1. Remove the 18 identifiers specified below, if present, that relate to the individual or relatives, employers, or household members of the individual; and

2. Have no actual knowledge that the remaining information could be used alone or in combination with other information held by the GWU researcher to identify a specific subject.

The 18 identifiers that must be removed, if present, are:

1. Names (initials do not have to be removed);
2. All geographic subdivisions smaller than a State, except for the first 3 digits of the zip code*;
3. All elements of dates (except year) directly related to an individual for those less than 89 years (ages < 89 years may be included in the data); all elements of dates (including year) for those over 89 years;
4. Telephone numbers;
5. Fax numbers;
6. Electronic mail addresses;
7. Social security numbers;  
8. Medical record numbers;  
9. Health plan beneficiary numbers;  
10. Account numbers;  
11. Certificate/license numbers;  
12. Vehicle identifiers and serial numbers, including license plate numbers;  
13. Device identifiers and serial numbers;  
14. Web Universal Resource Locators (URLs);  
15. Internet Protocol (IP) address numbers;  
16. Biometric identifiers, including finger and voice prints;  
17. Full face photographic images and any comparable images; \textit{and}  
18. Any other unique identifying number, characteristic, or \textit{code-link}.  

* The initial three digits of a zip code may be included in the data if, According to the current publicly available data from the Bureau of the Census, the geographic unit formed by combining all zip codes with the same three initial digits contains \textit{more than 20,000 people}; \textit{and} The initial three digits of a zip code for all such geographic units containing \textit{20,000 or fewer people} is changed to \textit{000}.  

IV. \textbf{Other HIPAA Issues}  

A. \textbf{Recruitment Issues Under HIPAA}  

1. \textbf{Creating a Recruitment Database}  

If a GWU CE-researcher wants to create a database of existing PHI to be used for subject recruitment in future studies, the Principal Investigator must submit a research protocol to the GWU IRB and request a \textit{waiver of research subject authorization} using the Waiver of Research Subject Authorization Request Form. Please note that the waiver of research subject authorization request applies only to data generated on or after April 14, 2003; any existing data (i.e., data generated prior to April 14, 2003) does not need a waiver of research subject authorization because such information is considered “grandfathered” under HIPAA. See below.  

2. \textbf{Secondary Use of Recruitment Databases}  

The Principal Investigator may use the PHI in the recruitment database to recruit subjects for specific research studies without obtaining an additional partial waiver of authorization. To disclose PHI in the recruitment database to other researchers for subject recruitment, the researchers must first obtain GWU IRB approval of a \textit{partial waiver of research subject authorization}. Please note that a request for partial waiver of research subject authorization applies only to data generated on or after April 14, 2003; any existing data (i.e., data generated prior to April 14, 2003) does not need a waiver of research subject authorization because such information is considered “grandfathered” under HIPAA.
The recipient researcher must destroy the identifiers of PHI from persons who are not enrolled in the study as soon as possible. The covered entity that maintains the database must disclose only the minimum PHI necessary to recruit subjects for the specific research protocol and must track the disclosures.

B. Research Databases or Specimen Repositories Issues Under HIPAA

1. Creating Databases/Repositories

Collection of PHI and/or biological specimens to create/maintain research databases/repositories is “research” under both the Common Rule and HIPAA. Under the Common Rule, collection of data or specimens with the prospective intent of storing the data or specimens for future research requires submission of a protocol to the GWU IRB for review and approval.

Under HIPAA, PHI and/or biological specimens may be collected from live subjects for inclusion in a database or repository only with a research subject authorization. If only existing PHI will be accessed to enter into a database, the research may qualify for a waiver of research subject authorization. See the following section for procedures to follow for subsequent (secondary) research of existing PHI or specimens stored in databases or repositories.

If biological specimens are collected from subjects without identifiers (anonymous), they are not PHI and are not subject to HIPAA requirements. Investigators involved in creating/maintaining specimen repositories should review the GWU, CHR, IRB Policy on Research Using Biological Specimens, which will be available at http://www.gwumc.edu/research/policies.htm

2. Research Using Existing Data or Biological Specimens

There are several mechanisms under HIPAA for using existing PHI in databases or biological specimens in stored repositories. They include:

PHI or specimens that were collected prior to April 14, 2003 under an IRB approved protocol (with informed consent or waiver of consent) or with a patient’s consent (e.g., surgical consent) that included future use for research may be used or disclosed by a covered entity for research with no additional HIPAA requirement. In these cases, HIPAA effectively ‘grandfathers’ authorization based on the prior consent.

PHI or specimens collected on or after April 14, 2003 may be used or disclosed by a covered entity for research with a waiver of research subject authorization if it poses no more than minimal risk to the subjects’ privacy. As a general rule, studies involving genetic testing of identified or identifiable biological specimens pose more than minimal risk to privacy and will not qualify for a waiver of research subject authorization.
PHI/specimens collected on or after April 14, 2003 may be used or disclosed by a covered entity for research with a research subject authorization if it poses more than minimal risk to the subjects’ privacy.

VII. Subject Rights Applied to Research

HIPAA requires covered entities to provide individuals rights to access their PHI and to know who has had access to their PHI and for what purpose their PHI was accessed. Only covered entities at GWU are required to comply with these HIPAA requirements.

A. Notice of Privacy Practices

GWU covered entities must provide patients who receive care at GWU a Notice of Privacy Practices (NPP) that describes how PHI is used or disclosed by the covered entity. These NPPs include references to research uses and disclosures of PHI. You can access the MFA and UHS NPP’s by contacting the Privacy Officer at each institution.

Many research subjects receive routine clinical care at GWU and will already have received an NPP prior to becoming a research subject. Subjects who have received a currently effective NPP do not need to receive another NPP when they enter a research protocol.

Subjects who have not previously been treated at GWU may need to receive an NPP if the research provides standard care along with the experimental procedures. For example, a clinical trial that provides standard tests that the subject would receive even if he/she were not in the protocol may generate bills to the subject/subject’s insurance carrier for that standard care. CE-researchers at GWU must provide such subjects with an NPP at the first point of contact and obtain the subject’s signed acknowledgment that the NPP has been received.

B. Subjects’ Rights to Access and Amend PHI

HIPAA allows patients to review and request amendment of any information that is contained in their Designated Record Set (DRS). A DRS is a group of records about a patient that the covered entity maintains to make decisions about the patient. The DRS normally will include medical and billing records and may include health plan enrollment, payment, claims adjudication and case or medical management records.

A clinical research record is not a DRS, however, research PHI may be entered into a DRS. For example, a protocol might involve blood tests and imaging studies that are part of standard care and that the subject would be receiving even if he/she were not in the study. This information is normally entered into the subject’s medical record as well as the research record. Once the information is entered into the medical record, it becomes part of the DRS.

Research subjects may request access to his/her DRS; however, for clinical trials, the PI may delay access to the DRS until the end of the study if such access would compromise a double blind protocol or otherwise be disallowed by the protocol for scientific reasons. If a subject’s
right to access his/her DRS will be suspended during the conduct of the clinical trial, the PI must inform subjects of that in the research subject authorization.

C. Accounting of Disclosures

GWU patients and research subjects have a right to receive an accounting of disclosures by covered entities of their PHI that have been made over the six years prior to the request (but not including disclosures prior to April 14, 2003). In general, this right applies to disclosures that the individual may not have known about or authorized. For research, the right applies to:

- Disclosures made pursuant to an IRB waiver or partial waiver of research subject authorization;
- Disclosures made under a Review Preparatory to Research;
- Disclosures made to or by Business Associates; or
- Disclosures made under a Request for PHI of Decedents.

The following types of research disclosures do not require an accounting:

- Disclosures made pursuant to a research subject authorization;
- Disclosures about the subject made to the subject;
- Disclosures of a limited data set with a data use agreement;
- Disclosures of de-identified data;
- Disclosures made to a subject’s insurance carrier for billing purposes;
- Disclosures made to a federal agency such as the FDA or NIH (if this was included in the RESEARCH SUBJECT AUTHORIZATION form);
- Disclosures made for adverse event reporting or similar data safety or monitoring purposes (if this was included in the RESEARCH SUBJECT AUTHORIZATION form); or
- Disclosures made for the purpose of treating the subject.

VII. Business Associate Agreements

A. Business associates in research

A Business Associate (BA) is a person or entity that performs a function for or on behalf of GWU covered entity involving the use or disclosure of the covered entity’s PHI. In general, sponsors, federal agencies or research collaborators (co-investigators at other institutions) are not BAs. Examples of BAs in research include:

1. A company that bills subjects or their insurance carriers for standard care procedures;
2. A company that provides telephone screening services for prospective research subjects;
3. A clerical service that transcribes or processes research data containing PHI.

Questions about whether an entity involved in a GWU research study is a BA should be directed to OHRCTT.
B. Negotiating Business Associate Agreements

GWU investigators may not negotiate BA Agreements. BA Agreements, like all research agreements, must be negotiated by GWU – not individual investigators – prior to initiating activities with the service provider.

BA Agreements must be negotiated by OHRCTT. GWU researchers who wish to enter into a BA Agreement must:

1. Obtain a template BA Agreement from OHRCTT;
2. Fill-in the necessary information and return the form to OHRCTT, 712 Ross Hall; and
3. Include information about the BA Agreement in the IRB Submission Form.

Ensure that a fully executed BA agreement is in place prior to the conduct of services or the sharing of PHI with the service provider.
APPENDIX A Glossary of Terms

**Adverse Event (AE)** – An undesirable experience concerning the health of a participant occurring during human subject research whether it is considered related to the study intervention.

**Advertising** – A method in which PIs recruit subjects for research studies.

**Alternatives** – Options available to subjects who are thinking about participating in research.

**Anonymity** – The inability to be named or identified by an individual on the basis of information provided to another.

**Assent** – The affirmative agreement by an individual, not competent to give legally valid informed consent, to participate in research.

**Assurance** – A formal written commitment that is submitted to OHRP in which an institution promises to comply with the Common Rule regulations (45 CFR Part 46) governing the protection of human subjects in research.

**Belmont Report** – A statement of basic ethical principles governing research involving human subjects that was issued in 1978 by the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research.

**Beneficence** – An ethical principle discussed in the Belmont Report that entails an obligation to protect persons from harm. The principle of beneficence can be expressed in two general rules: (1) do not harm; and (2) protect from harm by maximizing possible benefits and minimizing possible risks of harm.

**Benefit** – A valued or desired outcome; an advantage.

**Case-Control Study** – A study comparing persons with a given condition or disease (the cases), with persons without the condition or disease (the controls).

**Certificate of Confidentiality (COC)** – A document that protects the compelled release of identifiable information about research subjects in any legal proceeding. These documents are issued by the HHS and can be requested for all research, regardless of funding source.

**Children** – Persons who are minors as defined by district/state law.

**Clinical Investigation** – Any experiment that involves a test article and one or more human subjects that is subject to FDA regulations regarding research or marketing permits.

**Clinical Trial** – A controlled study involving human subjects designed to contribute to generalizable knowledge about the safety and effectiveness of an intervention or treatment, e.g., a new drug, new device, or a new behavioral intervention.
Coercion – The act of inducing or pressuring an individual to consent to participate in research or to stay in research.

Cognitive Impairment – A disorder that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished.

Competence – The capacity to act on one’s behalf, the ability to understand information presented, to appreciate the consequences of acting or not acting on that information, and to make a choice.

Confidentiality – The term pertains to the way a person treats information about another that has been disclosed by the individual to another in a relationship of trust and with the expectation that it will not be divulged to others without permission in ways that are inconsistent with the understanding of the original disclosure.

Control – Subject(s) used for comparison who are not given a treatment under study or who do not have a given condition, background, or risk factor that is the object of the study.

Continuing Review – The regulatory requirement that the IRB review research at intervals not greater than one year. The IRB may review research at more frequent intervals as desired.

Contract/Grant – Financial support provided for a research study designed and proposed by the PI. The financial support may come from either public or private funds.

Covered Entity – A health plan, health care clearinghouse, or health care provider who transmits health information in electronic form in connection with a HIPAA covered transaction.

Cross-Over Design – A type of clinical trial in which each subject experiences, at different times, both the experimental and control therapy.

Data and Safety Monitoring Board (DSMB) – A group of individuals responsible for collecting and analyzing information during the course of a clinical trial to monitor for adverse events and/or other trends. A DSMB looks for information that might warrant modification or termination of the trial or notification of subjects about new information that might affect their willingness to continue in the trial.

Data Gathering Instruments – Any instrument (e.g., survey, questionnaire) used during human subject research to collect data from a subject.

Dead Fetus – A fetus that fails to exhibit a heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, or pulsation of the umbilical cord.

Deception Study – A research study that incorporates in the design a technique for intentionally misleading a human subject during the course of the study to obtain certain results. The subject is debriefed after the study ends or after their participation ends.
**Declaration of Helsinki** – A code of ethics for clinical research approved by the World Medical Association. It has been widely adopted by medical associations worldwide and has been revised numerous times.

**De-Identified Protected Health Information** – PHI that has been stripped of 18 identifiers so that the health information is no longer individually identifiable.

**Delivery** – Complete separation of the fetus from the woman.

**Disclosure of Protected Health Information** – The release, transfer, provision of access to, or divulging in any other manner of protected health information outside the covered entity holding the information.

**Emancipated Minor** – A term, defined by state law, referring to the legal status of a person who has not yet attained the age of legal competency, but who is entitled to adult status for certain matters.

**Exemptions** – The Common Rule identifies six categories of research that involve human subjects that are exempted from the Common Rule regulations. FDA regulations contain an exemption from IRB review requirements for the emergency use of a test article (21 CFR 56.104(c)) and for certain taste and food quality evaluations and consumer acceptance studies (21 CFR 56.104(d)).

**Ex-Officio IRB Member** – A person who is listed on the GWU Medical IRB roster as a non-voting participant in IRB deliberations and actions.

**Expedited Review (ER)** – Review of proposed research by the IRB chair or a designated voting member rather than by review by the entire convened IRB. Federal regulations permit expedited review for: (1) certain kinds of research involving no more than minimal risk and that fall within a category listed on the November 9, 1998 Federal Register; and (2) for minor changes in previously approved research (45 CFR 46.110; 21 CFR 56.110).

**Experiment** – The testing of an intervention or interaction that is unproven and not yet scientifically validated.

**Fetus** – The product of conception from the time of implantation until delivery.

**Full Committee Review (FCR)** – Review of proposed research at a convened meeting of the IRB, at which a majority of the IRB members are present, including at least one member whose primary concerns are in a nonscientific area.

**Grant/Contract** – Financial support provided for a research study designed and proposed by the PI. Financial support may come from public or private funds.

**George Washington University (GWU)** – For the purposes of the Manual, the term GWU includes the faculty, staff, and students of GWU, GWU Hospital, and MFA.
Guardian – An individual authorized under applicable State/local law to consent on behalf of a minor to general medical care when general medical care includes participation in research.

Health Care Clearinghouse – For the purposes of HIPAA, this term means a public or private entity, including a billing service, re-pricing company, community health management information system or community health information system, and “value-added” networks and switches, that processes or facilitates the processing of health information received from another entity in a nonstandard format or containing nonstandard data content into standard data elements or a standard transaction or receives a standard transaction from another entity and processes or facilitates the processing of health information into nonstandard format or nonstandard data content for the receiving entity.

Health Care Provider – For HIPAA purposes, this term means a provider of services (as defined in section 1861(u) of the Act, 42 U.S.C. 1395x(u)), a provider of medical or health services (as defined in section 1861(s) of the Act, 42 U.S.C. 1395x(s)), and any other person or organization who furnishes, bills, or is paid for health care in the normal course of business.

Health Insurance Portability and Accountability Act (HIPAA) – A federal law that gives HHS the authority to mandate the use of standards for the electronic exchange of health care data; to specify what medical and administrative code sets should be used within those standards; to require the use of national identification systems for health care patients, providers, payers (or plans), and employers (or sponsors); and to specify the types of measures required to protect the security and privacy of personally identifiable health care information.

Historical Controls – Control subjects who are used for comparison with subjects being treated concurrently. A study is considered historically controlled when the present condition of subjects is compared with their own condition on a prior regimen or treatment.

Human in Vitro Fertilization – Any fertilization involving human sperm and ova that occur outside the human body.

Human Subject – According to Common Rule regulations, a human subject is a living individual about whom an investigator conducting research obtains data through intervention or interaction with the person or through individually identifiable private information. See 45 CFR 46.102(f). According to FDA regulations, a human subject includes an individual who is or becomes a participant in research, either as a recipient of a test article or as a control. A subject may be a healthy human/volunteer or a patient. See 21 CFR 50.3(g) and 56.102(e).

Incapacity – A person’s inability to understand information presented, to appreciate the consequences of acting (or not acting) on that information, and to make a choice.

Inclusion Criteria – Criteria that establish whether a person is eligible to participate in a trial.

Incompetence – A legal term meaning inability to manage one’s own affairs.
**Individually Identifiable Health Information** – Information that identifies, or reasonably may be used to identify, the individual including past, present or future information related to: (1) physical or mental health or conditions; (2) the provision of health care; or (3) the payment for the provision of health care.

**Information Sheet** – A written script of the informed consent information that is to be provided/presented (orally) to potential subjects when written documentation of informed consent is waived in accordance with federal regulations.

**Informed Consent** – A process that documents a person’s voluntary agreement, based upon adequate knowledge and understanding of relevant information, to participate in research or to undergo a diagnostic, therapeutic, or preventive procedure.

**Institutional Review Board (IRB)** – A review body established by regulation to protect the welfare of human subjects recruited to participate in research.

**Institutional Official** – The individual at an institution responsible for ensuring the effective administration and implementation of the institution’s system for protecting human subjects.

**Interaction** - Communications or interpersonal contact(s) between investigators (principal or sub) and subjects for research purposes.

**Intervention** - Physical procedures conducted by investigators on subjects by which data are gathered for research purposes. This term also includes manipulations to the subject or the subject’s environment that are performed by the investigators for research purposes.

**Investigational Device Exemption (IDE)** – Exemptions from certain FDA regulations that allow for the shipment of unapproved devices for use in clinical investigations. See 21 CFR 812.20.

**Investigational New Drug Application (IND)** – An application to conduct a clinical investigation involving a drug not yet determined by the FDA to be safe and effective for a particular use in the general population and not yet licensed for marketing. 21 CFR 312.1.

**IRB Member** – A person who is listed on the GWU Medical IRB roster as a voting participant in IRB deliberations and actions.

**Legally Authorized Representative (LAR)** – An individual or judicial or other body authorized under applicable law to consent on behalf of a prospective subject to the subject’s participation in the research procedure(s). For research purposes, only select states permit a LAR to consent for research participation 45 CFR 46.102(c); 21 CFR 50.3(e).

**Limited Data Set** – A subset of protected health information (PHI).

**Major Modification** - A change to an already approved research study that materially affects the risk vs. benefit ratio of the study, i.e., a change that increases the risk to the subject.
**Minimal Risk** – 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.

**Minor Modification** – A change to an already approved research study that does not materially affect the risk vs. benefit ratio of the study, i.e., a change that is of minimal risk to the subject.

**Monitoring** – A way of keeping track of any part of the research process, e.g., data analysis, recruitment of subjects, informed consent process, to ensure that the research remains in compliance with IRB conditions of approval and federal regulations.

**Neonate** – A newborn.

**Non-Affiliated Member** – Member of an IRB who has no ties (and whose immediate family members have no ties) to GWU, GWU Hospital, and/or MFA staff or faculty. Such non-affiliated members are usually from the local community. 45 CFR 46.107(d); 21 CFR 56.107(d).

**Non-Scientist** – Member of an IRB who does not have a scientific background, but may be affiliated with the institution. 45 CFR 46.107(c); 21 CFR 56.107(c). At least one non-scientist member must be present at convened meetings to approve research. See 45 CFR 46.108(b) and 21 CFR 46.108(c).

**Nonviable neonate** – A neonate after delivery that, although living, is not viable.

**Normal Volunteers** – Volunteer subjects in a research study who do not have the condition under study.

**Oral Consent** – Typically refers to informed consent that is obtained from a subject without use of a written informed consent document.

**Office for Human Research Protections (OHRP)** – An office within HHS that was created in June 2000. OHRP is responsible for enforcing the Common Rule regulations (45 CFR Part 46) governing the protection of human subjects in research. Prior to June 2002, this office was called the Office for Protection from Research Risks (OPRR). OPRR was part of the National Institutes of Health (NIH). OHRP replaces OPRR.

**Parent** – A child’s biological or adoptive parent.

**Permission** – The agreement of parent(s) or a guardian to research involving a minor. 45 CFR 46.402(c).

**Phase 1 Clinical Trials** – Phase 1 trials include the initial introduction of an investigational new drug into humans. These studies are typically conducted with healthy volunteers; however, where the drug is intended for use in patients with a particular disease, such patients may participate as subjects. Phase 1 trials are designed to determine the metabolic and pharmacological actions of the drug in humans, the side effects associated with increasing doses (to establish a safe dose
range), and, if possible, to gain early evidence of effectiveness. They are typically closely monitored. The ultimate goal of Phase 1 trials is to obtain sufficient information about the drug’s pharmacokinetics and pharmacological effects to permit the design of well-controlled, sufficiently valid Phase 2 studies. Other examples of Phase 1 studies include studies of drug metabolism, structure-activity relationships, and mechanisms of actions in humans, as well as studies in which investigational drugs are used as research tools to explore biological phenomena or disease processes. Typically, Phase 1 investigations involve anywhere from 20-80 subjects. 21 CFR 312.21(a).

**Phase 2 Clinical Trials** – Phase 2 trials include controlled clinical studies conducted to evaluate the drug’s effectiveness for a particular indication in patients with the disease or condition under study, and to determine the common short-term side effects and risks associated with the drug. These studies are typically well controlled, closely monitored, and conducted with a relatively small number of patients, usually involving no more than several hundred subjects. 21 CFR 312.21(d).

**Phase 3 Clinical Trials** – Phase 3 trials involve the administration of a new drug to a larger number of patients in different clinical settings to determine its safety, efficacy, and appropriate dosage. They are performed after preliminary evidence of effectiveness has been obtained, and are intended to gather necessary additional information about effectiveness and safety for evaluating the overall benefit-risk relationship of the drug, and to provide an adequate basis for physician labeling. In Phase 3 studies, the drug is used the way it would be administered when marketed. When these studies are completed and the sponsor believes that the drug is safe and effective under specific conditions, the sponsor applies to the FDA for approval to market the drug. Phase 3 trials usually involve several hundred to several thousand subjects. 21 CFR 312.21(c).

**Phase 4 Clinical Trials** – The FDA, when it gives market approval, may seek an agreement from the sponsor to conduct certain post-marketing studies to ascertain additional information about the drug’s risks, benefits, and optimal use. These studies could include, but would not be limited to, studying different doses or schedules of administration than were used in Phase 2 studies, use of the drug in other patient populations or other stages of the disease, or use of the drug over a longer period of time. 21 CFR 312.85.

**Protected Health Information** – HIPAA defines this term to include individually identifiable health information that is transmitted by electronic media, or transmitted or maintained in any other form or medium.

**Placebo** – A chemically inert substance given in the guise of medicine for its psychologically suggestive effect; used in controlled clinical trials to determine whether improvement and side effects may reflect imagination or anticipation rather than the actual power of a drug.

**Pregnancy** – The period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery.
**Principal Investigator (PI)** – The person with primary responsibility for design and conduct of a research project.

**Prisoner** – An individual involuntarily confined or detained in a penal institution, including persons: (1) sentenced under a criminal or civil statute; (2) detained pending arraignment, trial, or sentencing; and (3) detained in other facilities (e.g., for drug detoxification or treatment of alcoholism) under statutes or commitment procedures providing such alternatives to criminal prosecution; or (4) incarcerated in a penal institution [45 CFR 46.303(c)].

**Privacy** – Concealment from others of information about oneself.

**Prospective Studies** – Studies designed to observe outcomes or events that occur subsequent to the identification of the group of subjects to be studied. Prospective studies need not involve manipulation or intervention but may be purely observational or involve only the collection of data.

**Protocol** – The formal design or plan of an experiment or research activity. The protocol includes a description of the research design or methodology to be employed, the eligibility requirements for prospective subjects and controls, the treatment regimen(s), and the proposed methods of analysis that will be performed on the collected data.

**Quorum** – The majority of IRB members being present at a FCR IRB meeting

**Random Assignment** – Assignment of subjects to different treatments, interventions, or conditions according to chance.

**Recruitment** – The process of enrolling human subjects in research protocols.

**Remuneration** – Refers to payment or other benefits that will be given to subjects who volunteer to participate in research protocols.

**Research** – According to the Common Rule research is a systematic investigation/study, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. 45 CFR 46.102(d). Pursuant to FDA regulations, research is any use of a FDA regulated product except for use of a marketed product in the practice of medicine. Research is also said to be synonymous with clinical investigation.

**Research Coordinator** – A member of the research team that is responsible for coordinating all research related activities including, but not limited to the submission of regulatory documents to the IRB, sponsor, federal regulatory agencies, drafting informed consent forms, conducting data analysis, etc.

**Respect for Persons** – A principle enunciated in the Belmont Report stating that (1) individuals should be treated as autonomous agents, and, (2) persons with diminished autonomy are entitled to protection.
**Retrospective Studies** – Research conducted by reviewing records from the past (e.g., birth and death certificates, medical records, etc.) or by obtaining information about past events elicited through interviews or surveys, e.g., case control studies.

**Risk** – The probability of harm or injury occurring as a result of participation in a research study.

**Serious Adverse Event** - An adverse event that results in any of the following: death, a life-threatening adverse drug experience (see above), inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or a congenital anomaly/birth defect.

**Site Visit** – Typically refers to a visit from a federal office to ensure the entity is complying with federal regulations.

**Sponsor** – Typically refers to the entity that initiates a clinical investigation but does not actually conduct the investigation [21 CFR 50.3(e) and 56.102(j)].

**Sponsor-Investigator** – An individual who both initiates and actually conducts a clinical investigation [21 CFR 50.3(f) and 56.102(k)].

**Sub-Investigator** – For the purposes of this manual, this term includes all investigators associated with a particular study, excluding the principal investigator.


**Subpart B of CFR Part 46** – This subpart contains additional protections for pregnant women and fetuses that are involved in research, and references human in vitro fertilization research.

**Subpart C of CFR Part 46** – This subpart contains additional protections for prisoners who are involved in research.

**Subpart D of CFR Part 46** – This subpart contains additional protections for children who are involved in research.

**Surveys** – A way to obtain data gathering information from human subjects through written questionnaires, telephone interviews, door-to-door canvassing, or similar procedures.

**Suspension** – Typically used in the context of a federal agency taking action against an institution. For example, the Office for Human Research Protections can suspend an Assurance, preventing the institution from continuing to conduct studies supported with federal funds.

**Test Article** – Any drug, biological product for human use, medical device for human use, human food additive, color additive, electronic product subject to FDA regulations.
**Unanticipated Problems Involving Risks to Subjects or Others** – This is a regulatory phrase that requires reporting of this event to the IRB and to the government 45 CFR 46.103(d)(5); 21 CFR 56.108(b).

**Use of Protected Health Information** – This includes the sharing, employment, application, utilization, examination, or analysis of PHI within the covered entity that maintains the PHI.

**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.

**Voluntary** – Free of coercion, duress, or undue influence.

**Vulnerable population** – This is a regulatory phrase that refers to a group of people who have some condition or situation that makes them more susceptible to coercion or undue influence. 45 CFR 46.107(a).

**Waiver of Informed Consent** – An action taken by the IRB permitting the investigator to pursue research involving human subjects without obtaining informed consent. 45 CFR 46.116(d) & 46.117(c).

**Ward** – A child who is placed in the legal custody of the State or other agency, institution, or entity, consistent with applicable Federal, State, or local law.
APPENDIX B Differences in FDA and HHS Regulations for Protection of Human Subjects

The Department of Health and Human Services (HHS) regulations [45 CFR Part 46] apply to research involving human subjects conducted by HHS (or one of the other federal departments/agencies that have adopted the Common Rule) or funded, in whole or in part, by HHS (or one of the other federal departments/agencies that have adopted the Common Rule). The Food and Drug Administration (FDA) regulations [21 CFR Parts 50 and 56] apply to research involving products regulated by FDA. Federal support is not necessary for the FDA regulations to be applicable. Both HHS and FDA regulations apply when research involves products that are regulated by FDA and the research is funded, supported or conducted by FDA and/or HHS (or one of the other federal departments/agencies that have adopted the Common Rule). The information provided below comes from FDA INFORMATION SHEETS 1998 UPDATE.

IRB Regulations

<table>
<thead>
<tr>
<th>Section Numbers</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>56.102 (FDA)</td>
<td>FDA definitions are included for terms specific to the type of research covered by the FDA regulations.</td>
</tr>
<tr>
<td>46.102 (HHS)</td>
<td>FDA regulations (test article, application for research or marketing permit, clinical investigation). A definition for emergency use is provided in the FDA regulations.</td>
</tr>
<tr>
<td>56.104 (FDA)</td>
<td>FDA provides exemption from the prospective IRB review requirement for &quot;emergency use&quot; of test article in specific situations.</td>
</tr>
<tr>
<td>46.116 (HHS)</td>
<td>HHS regulations state that they are not intended to limit the provision of emergency medical care.</td>
</tr>
<tr>
<td>56.105 (FDA)</td>
<td>FDA provides for sponsors and sponsor-investigators to request a waiver of IRB review requirements (but not informed consent requirements).</td>
</tr>
<tr>
<td>46.101 (HHS)</td>
<td>HHS exempts certain categories of research and provides for a Secretarial waiver.</td>
</tr>
<tr>
<td>56.109 (FDA)</td>
<td>Unlike HHS, FDA does not provide that an IRB may waive the requirement for signed consent when the principal risk is a breach of confidentiality because FDA does not regulate studies, which would fall into that category of research. (Both regulations allow for IRB waiver of documentation of informed consent in instances of minimal risk.)</td>
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<tr>
<td>46.109 (HHS)</td>
<td></td>
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<tr>
<td>46.117(c)(HHS)</td>
<td></td>
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<tr>
<td>56.110 (FDA)</td>
<td>The FDA list of investigations eligible for expedited review (published in the Federal Register) does not include the studies described in category 9 of the HHS list because these types of studies are not regulated by FDA.</td>
</tr>
<tr>
<td>46.110 (HHS)</td>
<td></td>
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<tr>
<td>56.114 (FDA)</td>
<td>FDA does not discuss administrative matters dealing with grants and contracts because they are irrelevant to the scope of the Agency's regulation. (Both regulations make allowances for review of multi-institutional studies.)</td>
</tr>
<tr>
<td>46.114 (HHS)</td>
<td></td>
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<tr>
<td>56.115 (FDA)</td>
<td>FDA has neither an assurance mechanism nor files of IRB membership. Therefore, FDA does not require the IRB or institution to report changes in membership whereas HHS does require such notification.</td>
</tr>
<tr>
<td>46.115 (HHS)</td>
<td></td>
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<tr>
<td>56.115(c) (FDA)</td>
<td>FDA may refuse to consider a study in support of a research or marketing permit if the IRB or the institution refuses to allow FDA to inspect IRB records. HHS has no such provision because it does not issue research or marketing permits.</td>
</tr>
<tr>
<td>56.120 ----</td>
<td>FDA regulations provide sanctions for non-compliance with regulations.</td>
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<tr>
<td>56.124 (FDA)</td>
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### Informed Consent Regulations

<table>
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<tbody>
<tr>
<td>ß 50.23 (FDA)</td>
<td>FDA, but not HHS, provides for an exception from the informed consent requirements in emergency situations. The provision is based on the Medical Device Amendments of 1976, but may be used in investigations involving drugs, devices, and other FDA regulated products in situations described in ß 50.23.</td>
</tr>
<tr>
<td>ß 46.116(c)&amp;(d) (HHS)</td>
<td>HHS provides for waiving or altering elements of informed consent under certain conditions. FDA has no such provision because the types of studies, which would qualify for such waivers, are either not regulated by FDA or are covered by the emergency treatment provisions (ß 50.23).</td>
</tr>
<tr>
<td>ß 50.25(a)(5) (FDA)</td>
<td>FDA explicitly requires that subjects be informed that FDA may inspect the records of the study because FDA may occasionally examine a subject's medical records when they pertain to the study. While HHS has the right to inspect records of studies it funds, it does not impose that same informed consent requirement.</td>
</tr>
<tr>
<td>ß 46.116(a)(5) (HHS)</td>
<td>FDA explicitly requires that consent forms be dated as well as signed by the subject or the subject's legally authorized representative. The HHS regulations do not explicitly require consent forms to be dated.</td>
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