Parker University
Institutional Review Board
Standard Operating Procedures
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1. Institutional Authority

The administration of Parker University (PU) has established one internal Institutional Review Board (IRB) to review all human subjects research. The PU-IRB is required to meet at least once each year, although more frequent meetings may be scheduled. Institutional oversight of the IRB is the responsibility of the PU administrator responsible for research.

The administration of Parker University delegates the responsibility of instituting, monitoring and evaluating all investigational research carried out in PU. The IRB is given the authority to approve, disapprove or require modification of proposed studies upon consideration of the protection and welfare of human research subjects. The IRB is also given the authority to suspend, terminate or restrict studies. The IRB is given the authority to require progress reports and oversee the conduct of the study. The ultimate responsibility for the appropriateness of IRB activity shall rest with the Provost, who may reserve the right to reverse actions taken by the IRB to approve initiation of investigational research but may not approve research for investigation which have been rejected by the IRB. Reports regarding IRB activity shall be made to the administration through the PU administrator responsible for research.

2. Purpose

The PU-IRB is formally designated to review, approve the initiation of, and conduct periodic review of any research studies being carried out at PU which involve human subjects. The primary function of the IRB is to maximize the protection and welfare of the human subjects involved in any research study. Any clinical investigation involving a reasonable expectation that a human subject of research will receive treatment at a PU entity must first be reviewed and approved by, and remain subject to continued monitoring, by the PU-IRB. The IRB is governed by all applicable regulations enforced by the Department of Health and Human Services (DHHS), Food and Drug Administration (FDA), National Institutes of Health (NIH), all other federal, state and local laws (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe), rules and regulations applicable to the conduct of research, and the principles of the Belmont Report.

The PU-IRB also informs and assists PU and its researchers on ethical and procedural issues related to the use of human subjects in research, to facilitate compliance with relevant regulations of the United States Government and relevant state and local law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe), and to provide a framework suitable for continued support by government agencies, private foundations and the industry for research involving human subjects at PU.

Primary responsibility for assuring the protection of the rights and welfare of the individuals involved in research rests with principal investigators conducting the research. Others engaged in the conduct of the research share this responsibility. Educational faculty, from both outside and inside PU, who assign or supervise research conducted by students or staff have an obligation to consider carefully whether those individuals are qualified to adequately safeguard the rights and welfare of subjects.
3. The Scope & Authority of the IRB

Scope
All human subjects research carried out at PU or under its auspices must be reviewed and approved by the PU-IRB prior to the start of the research. The IRB is guided by the principles of the Belmont Report and the Common Rule in reviewing all human subjects protocols.

Authority for the IRB oversight of all federally-funded research is provided in the regulations of the Department of Health and Human Services (DHHS) at 45 CFR 46. Authority for IRB oversight of all research with products regulated by the FDA is provided in 21 CFR 50 and 56.

PU-IRB reviews projects when:

1. the research is sponsored by PU;
2. the research is conducted by or under the direction of any employee or agent of PU (including students and chiropractic and other staff) in connection with his or her institutional responsibilities;
3. the research is conducted by or under the direction of any employee or agent of PU (including students and chiropractic and other staff) using any property or facility of this institution;
4. the research is conducted by or under the direction of any employee or agent of PU (including students and chiropractic and other staff) that meet the criteria for “engaged in research” as defined in OHRP guidance dated October 16, 2008;
5. the research involves the use of PU non-public information to identify or contact human subjects; and/or
6. upon request and at their discretion, the PU-IRB agrees to review additional research projects not fitting the criteria above.

Exceptions can be made if it is determined by the Human Protections Administrator, the IRB Chair or his/her IRB member designee that PU is not engaged in research. The PU-IRB may be convened on an “as-needed” basis for the specific purpose of reviewing reports of noncompliance, to make policy determinations, or to conduct additional project reviews. These convened full-board meetings are scheduled so that the majority of those in attendance are the voting members of the PU-IRB.

Authority of the PU-IRB

The authority conveyed to the PU-IRB includes the following:

1. Review all research projects involving human subjects before the involvement of human subjects may begin including exempt research activities for which limited IRB review is a condition of exemption;
2. Require from investigators modifications in research protocols, informed consent documents, and/or recruitment materials as a condition for initial or continuation approval;

3. Approve or disapprove new research projects and the continuation of previously approved projects;

4. Require that information given to subjects (or legally authorized representatives, when appropriate) as part of informed consent is in accordance with federal regulations and institutional policies. The IRB may require that additional information be given to the subjects when in the IRB’s judgment the information would meaningfully add to the protection of the rights and welfare of subjects.

5. Require documentation of informed consent or waive documentation in accordance with federal regulations.

6. Monitor the activities in approved projects including regularly scheduled continuing review at least every twelve months, verification of compliance with approved research protocols and informed consent procedures, and observation (or third-party observation) of the consent process;

7. Develop mechanisms for prompt reporting to the IRB of any planned changes in approved projects prior to the implementation of those changes;

8. Develop mechanisms for prompt reporting to the IRB of any unanticipated problems involving risks to subjects or others occurring in approved projects, or in other projects related in context to the approved projects;

9. Suspend or terminate a previously approved project;

10. Restrict aspects of a research study for the purpose of subject protection;

11. Review and monitor the use of test articles (investigational drugs, biologicals and devices, including Humanitarian Use Devices) for the purpose of treatment of serious or life-threatening illnesses. This is unlikely to take place at Parker University.

**Authority of the Institutional Official**

The PU administrator responsible for research, as the designated Institutional Official, has the authority to review decisions of the IRB. In the case of an approval decision, should the PU administrator responsible for research conclude that a project does not fully comply with policies or obligations of PU, s/he may disapprove, suspend, or terminate the project on behalf of the institution. In the case of a decision by the IRB to disapprove, suspend, or terminate a project, the decision may not be reversed by any other person or entity including the PU administrator responsible for research or any other officer/agency of PU, or state, local, tribal or federal government.

**Undue Influence**

All IRBs must be autonomous in their decision-making and determinations. The Provost’s office upholds the independence of the PU-IRB from external influences. Additionally, the IRB Chair fosters an environment that encourages the free and full participation of all
members in the deliberations of the committee. Investigations of attempts to unduly influence any member of the PU-IRB or IRB administrative support staff will focus on the protection of the independence of the IRB members and support staff so that they can function in the role of protecting research participants. Attempts to unduly influence the IRB can be reported in the following manner.

1. When a member experiences undue influence, s/he should report such an occurrence to the Human Protections Administrator (HPA) or to the IRB Chair. These reports of undue influence go to the PU administrator responsible for research. If the staff member feels that undue influence is coming from either the HPA or IRB Chair, s/he reports the occurrence to the PU executive responsible for research directly. If the staff member feels the undue influence is coming from any of the above individuals in the reporting chain, the staff member can report the incident to the Human Resources Department.

2. When an IRB member experiences undue influence, s/he should first report the occurrence to the IRB chair. The IRB chair can then notify the HPA. The report then goes to the Provost. If the IRB member feels that the undue influence is coming from the IRB chair, or the HPA, the IRB member reports directly to the Provost. If the IRB member experiences undue influence from any of the above reporting chain, the IRB member can report the incident to the HR Department.

Parties to whom the reports are made will evaluate the allegation and will determine a course of action to be taken. Actions can include additional investigation, internal resolution, or referral to the Provost, President of PU or the HR Department, as appropriate.

4. Relationship of the PU-IRB to Other Entities

Compliance with Federal and State Regulations

PU filed a Federalwide Assurance (FWA) with the DHHS Office for Human Research Protections (OHRP) affirming that Parker complies with 45 CFR 46 (Common Rule). This assurance applies to all research involving human subjects funded by federal agencies subscribing to the Common Rule. The full text of the FWA is available in hard copy by contacting the HPA.

In studies involving products regulated by the FDA regulations, the PU-IRB complies with the requirements set forth in 21 CFR 11 (Electronic Signatures), 21 CFR 50 (Protection of Human Subjects), 21 CFR 56 (Institutional Review Boards), and 21 CFR 812 (Investigational Device Exemptions). Parker University does not conduct drug research.

The PU-IRB operates as a Privacy Board as described in the Standards for Privacy of Individually Identifiable Health Information, also known as the Privacy Rule, (45 CFR 160 and 164) of the Health Insurance Portability and Accountability Act (HIPAA) when research involves protected health information as described in this act.
For any research under the authority of the PU-IRB, the IRB may confer with the PU legal counsel regarding the applicability of local, state tribal, national, or international laws to the particular study. The PU-IRB will apply the law of the state in which the research is being conducted. For example, if a project involves children and one of the recruitment sites is in a bordering state, the laws of the bordering state will be evaluated to which individuals meet the DHHS and FDA definition of “children” at that site.

**Cooperative Research and IRB Reliance Agreements**

In the conduct of cooperative research projects (i.e., projects that involve more than one institution), each institution (or entity) is responsible for safeguarding the rights and welfare of human subjects and for complying with any applicable regulations. This applies to all nonexempt research involving human subjects or exempt research for which limited IRB review is required. Federal regulations from DHHS and FDA (45 CFR 46.114 & 21 CFR 56.114) allow for cooperative research projects which involve more than one institution. To avoid duplication of review efforts by IRBs, the PU-IRB can choose to conduct joint reviews, rely upon the review of another qualified IRB, or make other arrangements to establish oversight responsibilities. PU makes a determination about whether or not a cooperating outside institution is also engaged in human subjects research in collaboration with PU. This determination is made by the Human Protections Administrator or the PU-IRB Chair (or IRB member designee) based on the outside institution’s role and whether that role meets any of the criteria for “engaged in research” as defined in OHRP guidance dated October 16, 2008.

1. When the outside institution is determined to be engaged and is receiving federal funds through a subcontract with PU, the PU-IRB requires documentation that the outside institution holds an FWA through the subcontract process. If the outside institution does not hold its own FWA, PU requires that they obtain one prior to finalization of the subcontract. Under limited circumstances, when PU is able to assure understanding of local context in relation to the proposed research and has sufficient resources to provide appropriate oversight during the conduct of the research, PU may choose to extend its FWA to cover the outside institution’s role in this single project.

2. When the outside institution is determined to be engaged, but is not receiving federal funding for the study through a subcontract with PU, the PU-IRB requires that the research be conducted under another entity’s IRB oversight or PU-IRB's oversight. In the former instance, the PU-IRB will require documentation that the outside IRB will provide this oversight. In the latter instance, a formal IRB Reliance Agreement will be required. The PU-IRB will oversee research for an outside institution only when the PU-IRB is able to assure understanding of local context in relation to the proposed research and has sufficient resources to provide appropriate oversight during the conduct of the research.

When the outside institution is determined to be engaged as described in 1 or 2 above, and PU determines that the outside institution’s IRB review will provide more appropriate expertise, oversight, and/or knowledge of local context for PU’s role in the study, PU may choose to enter
into an IRB Reliance Agreement or other equivalent agreement to make the non-local IRB (or External IRB) the IRB of record for that particular study. When this occurs and the research is federally funded, the external IRB is added to the PU FWA.

When PU and an outside institution agree to use a single IRB to review a cooperative research project, an IRB Reliance Agreement will be developed documenting the responsibilities that each entity will undertake to ensure compliance with federal and institutional regulations. The final determination to enter into any agreements described in this section is made by the Institutional Official (i.e., PU administrator responsible for research).

**National Institutes of Health Policy on the Use of a Single Institutional Review Board**

Effective January 25, 2018, all sites participating in multi-site studies involving nonexempt human subjects research funded by the NIH will be required to use a single Institutional Review Board (sIRB) to conduct the ethical review required by the Department of Health and Human Services regulations for the Protection of Human Subjects at 45 CFR Part 46. This policy, which is consistent with 45 CFR Part 46.114, is intended to enhance and streamline the process of IRB review and reduce inefficiencies so that research can proceed as expeditiously as possible without compromising ethical principles and protections for human research participants.

This policy applies to all domestic sites of NIH-funded multi-site studies where each site will conduct the same protocol involving non-exempt subjects research whether supported through grants, cooperative agreements, contracts, or the NIH Intramural Research Program. It does not apply to career development, research training or fellowship awards.

**Common Rule Single IRB Requirement (45 CFR 46.114)**

Effective January 19, 2020, any institution located in the United States that is engaged in cooperative research conducted by a department or agency that has adopted the Common Rule (45 CFR 46.114), must rely upon approval by a single IRB for that portion of the research that is conducted in the United States. The reviewing IRB will be identified by the Federal department or agency supporting or conducting the research or proposed by the lead institution subject to acceptance of the Federal department or agency supporting the research.

The following research is not subject to the requirement for single IRB use:

1. Cooperative research for which more than single IRB review is required by law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe); or

2. Research for which any Federal department or agency supporting or conducting the research determines and documents that the use of a single IRB is not appropriate for the particular context.
External IRB Policy

Researchers should detail the process for information flow between the IRB of Record and Relying IRB throughout the lifecycle of the initial protocol review, amendments, reporting, continuing review and study closure. This includes responsibilities for the IRB of Record, Relying IRB(s), lead study team, and the relying study team(s).

5. The PU-IRB Membership and Responsibilities

Appointment of Members

The IRB, in consultation with the HPA, will recommend membership to the Provost. The length of the appointment is two years, and membership can be reappointed indefinitely.

The PU-IRB Chair and Vice-Chair

The PU-IRB has a Chair and a Vice Chair. These individuals are respected, active members of the Parker community who are well-informed in regulations relevant to the use of human subjects in research. The Provost will appoint new members to the IRB. Factors that will be considered in the nomination process include the candidate’s experience in human research protections, professional discipline(s) and achievements, educational background, and his or her availability to commit the appropriate amount of time and effort to the PU-IRB program. The term of service is two years. Chair and Vice-Chair can be re-nominated and serve an unlimited amount of consecutive terms.

Whenever a Chair or Vice Chair is not available to conduct the PU-IRB business, s/he may designate a board member to assume his/her responsibilities during the period of his/her absence. An IRB Chair designee will be a named member of the IRB.

Responsibilities of the IRB Chair include:

1. Determining the type of review for initial, continuing review, and modification applications (exempt, expedited, full board) based on regulatory criteria,
2. Conducting expedited reviews and approvals,
3. Assigning primary reviewers for PU-IRB applications,
4. Running full board meetings,
5. Reviewing minutes,
6. Reviewing specific revisions to protocols/consent documents that are required as conditions of approval,
7. Reviewing reports of unanticipated problems involving risks to subjects or others, and
8. Approving the use of a test article in emergency situations

In addition, the Chair and Vice-Chair will serve as resources for investigators and the PU-IRB members regarding issues related to the PU-IRB, federal, state, local and tribal regulations.
**Regular Members**

The PU-IRB has at least five members including at least one member whose primary concerns are in scientific areas and at least one member whose primary concerns are in nonscientific areas. The PU-IRB members are selected with varying backgrounds of expertise, experience, and diversity to promote complete and adequate review of research activities commonly conducted by the institution. The PU-IRB includes at least one member who is not otherwise affiliated with the institution.

Membership rosters are maintained by the HPA and reviewed on an ongoing basis by the Provost and HPA to assure that expertise and experience is representative of the research under review. When a deficiency is identified, the HPA conducts directed recruitment of individuals with the needed expertise or experience. Recommendations for IRB membership may come from the PU-IRB Chair, PU-IRB members, Provost, or others. Before a formal offer can be extended, the nominee must be approved by the Provost.

**Alternate IRB Members**

Alternate IRB members may be recommended by the IRB and appointed by the PU Administration. Alternate IRB members, if appointed, are designated for a specific member or members. Alternate IRB members are selected to assure comparable qualifications to the primary member based on discipline, expertise, and/or education and professional experience as appropriate. In the absence of the designated IRB member, the alternate may attend the meeting as a voting IRB member. If both the alternate IRB member and the primary IRB member attend a meeting, only one of these two may vote. In these cases, the minutes reflect who is in attendance as a voting IRB member. The alternate IRB member will have a reasonable opportunity to review the agenda material on which they are being asked to vote.

**Non-Voting Members**

The IRB Chair may, at his/her discretion, recruit non-voting (*ex officio*) members whose presence at the meetings of the PU-IRB would aid the IRB in conducting their duties. These members may take part in all meetings of the IRB, participate in the discussions, and make recommendations, but they may not vote on the decisions. Non-voting members are not included in determining or establishing a quorum at the meetings. The PU-IRB meeting minutes reflect the presence of non-voting members.

**Consultants/Ad hoc Reviewers**

At its discretion, the PU-IRB may invite scientists or non-scientists from within or outside PU, who have special expertise, to function as consultants and *ad hoc* reviewers of a study.
application. These individuals have access to all documents submitted to the PU-IRB relevant to the specific project under review, may participate in the deliberations and make recommendations on the project, but may not vote.

**IRB Member Responsibilities**

Responsibilities of members include reviewing human subject application materials in advance of meetings and being prepared to discuss issues related to human subjects protections, serving as primary reviewer when requested by the Chair, and having an understanding of the specific requirements of human subjects regulations. Members who do not adequately fulfill their responsibilities as judged by the PU-IRB Chair may be asked to step down from PU-IRB membership by the IRB Chair or the Provost.

The Provost can remove people from the IRB.

**Conflicts of Interest**

No PU-IRB member, consultant, or ad hoc reviewer may participate in the IRB review of any project in which the member has a conflict of interest or any other relationship that may be inappropriate for objective review, except to provide information requested by the Board. The individual can be a member of the PU-IRB; however, s/he cannot participate in the review and approval process for any project in which s/he has a conflict of interest. This conflict of interest policy includes all types of review (i.e., review by expedited procedures, review by a convened IRB, review of unanticipated problems involving risks to participants or others, or review of noncompliance with the regulations or requirements of the IRB). In cases where the assigned initial reviewer has a conflict of interest, that study application is re-assigned to another reviewer or taken to the full Board. When the investigator-member has a conflicting interest, s/he may be present at the PU-IRB meetings, like any investigator, only to provide information requested by the Board. S/He, at the discretion of the IRB Chair or designee, may be asked to leave the meeting room during the subsequent discussion and voting phases of the review and may not vote (e.g., agree, disagree, abstain) on the study. The absent member is not counted towards a quorum when the vote on the study in question is taken. Meeting minutes document that these requirements have been met.

**Scheduling of Meetings**

The PU-IRB is scheduled to meet monthly, less if there is no business to conduct. A schedule can be provided upon request to the HPA. Between 10-14 days prior to the full Board meeting a prep meeting may be held with the HPA and the IRB Chair and/or Vice-Chair of the IRB. At this meeting the IRB agenda is set and applicable submissions are expedited.

Individual meetings of the IRB may be cancelled by the IRB Chair due to a) insufficient applications requiring full Board review, b) holiday, c) inability to secure a quorum for attendance, or d)
other reasons as may arise that make a scheduled meeting unnecessary or otherwise inappropriate.

**Notification of Meetings and Distribution of Materials**

The agenda and application materials are distributed to all PU-IRB members sufficiently in advance of the meeting date to allow time for review, generally a week in advance. The agenda indicates the date, time, and place of the meeting. For full Board meetings, all attending PU-IRB members, and identified consultants, if applicable, receive access via email to documents, including but not limited to the application form, study protocol, informed consent document(s), recruitment materials (including direct advertising materials), other proposed correspondence with subjects (if applicable), progress or status reports for continuing reviews, and other materials as determined by the Chair (as applicable). All IRB members scheduled to attend a meeting are expected to review all materials in sufficient depth to discuss the information at the convened meeting.

**Urgent Review of Applications**

Urgent review procedures may be invoked only under unusual circumstances with the approval of the HPA or IRB Chair. This does not include urgency that is a result of negligence or delay on the part of the investigator or his/her staff to submit research-related applications in a timely fashion.

If the HPA or IRB Chair permits urgent review of an application, the materials are distributed as soon as possible to the PU-IRB members to allow as much time as possible for review prior to the meeting. The investigator may be required to attend the meeting to answer any questions that arise.

**Meeting Procedures**

The PU-IRB meetings are called to order when a quorum of members is in attendance. A quorum consists of one more than half of the primary members and must include at least one person whose primary interest is in a non-scientific area. The meeting ends or is suspended whenever a quorum of members is no longer present. If a prisoner advocate is present, s/he counts as a primary member and the number of members required for a quorum may change. The quorum is monitored throughout the meeting by a member of the HPA or the IRB Chair.

At the discretion of the IRB Chair and/or Primary Reviewer, the investigator(s) may be invited to attend the meeting for the purpose of additional clarification or discussion. The investigator(s) is (are) required to leave the meeting for subsequent discussion and voting.

At the discretion of the IRB Chair, voting may be by voice, written ballot or a show of hands.
The official meeting minutes record a motion from the Board, a seconded motion from the Board and the number of votes which agree or disagree with the motion as well as the number abstaining.

A majority vote of the members present at the meeting is required for approval. Investigators are notified via email of the decision of the PU-IRB and any changes required in their study application.

**Meeting Minutes**

Minutes are generated that record the following information:

1. Attendance at each meeting including those members or alternate members who participated through videoconference or teleconference;
2. Indication by name when members are absent from voting due to a conflict of interest on individual agenda items or when they are not present for discussion and voting on individual agenda items;
3. The presence of any invited investigators or guests
4. The vote on actions taken by the IRB including the number, for, against and abstaining;
5. Separate deliberations for each action, where applicable;
6. Reasons for requiring modifications to secure approval of a research protocol, for disapproving a research protocol, or suspending or terminating a research protocol;
7. The length of time of an approval;
8. A written summary of the discussion of controverted issues and their resolution;
9. If pregnant women, fetuses, prisoners, or children are involved in the research, protocol specific findings about their inclusion, the additional specific safeguards, the procedures for consent, parental permission or assent of children and other determinations required by the federal regulations.
10. If an investigational device is included in the research, a categorization of the device as either a Significant Risk (SR) device or a Non-Significant Risk (NSR) device;
11. Where appropriate, information regarding expedited approvals, modifications, terminations, emergency/single patient use, unanticipated problems involving risks to subjects or others, and any other business appropriate for Board meetings;
12. If the convened IRB approves research contingent on specific minor conditions and the HPA, IRB Chair, or another IRB member designated by the Chair approves the modifications, the approval by the Chair or designee is documented in the minutes of the first IRB meeting that is convened after the date of approval.

A copy of the minutes is provided to the Parker IRB members for review before the next meeting. At the actual Parker IRB meeting, members have an opportunity to request clarifications or suggest changes to the minutes. Suggested modifications to the minutes are discussed at a convened meeting and agreed to by consensus, and the minutes are subsequently modified according to the IRB’s recommendations by HPA staff, with the Board providing a final review and approval. When the Board approves the minutes, they
become the official minutes for that Parker IRB meeting. After approval by the IRB, the minutes cannot be altered by anyone including a higher authority, unless the PU-IRB approves and documents the change.

Tabled Studies

When a study is tabled at a meeting (i.e., the majority vote agrees with a motion to table), the study must be returned to a full Board IRB meeting for review. The full Board meeting procedures described above are followed for these protocols. Additional materials distributed to members for tabled studies include the minutes from the previous meeting and any response to those minutes from the investigators.

Suspension or Termination of IRB Approval

The PU-IRB has the authority to suspend or terminate approval of human subjects research that is not being conducted in accordance with the PU-IRB requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval includes a statement of the reasons for the IRB’s action and is reported in writing within 5 working days to the investigator.

Suspensions implemented by the IRB Chair will be reported to and reviewed by the convened IRB. The IRB may take actions, within its authority, as deemed appropriate.

When suspending or terminating IRB approval on an urgent basis, the IRB (or IRB chair for suspensions) must:
1. Consider actions to protect the rights and welfare of currently enrolled participants;
2. Consider whether participants should be informed of the termination or suspension; and
3. Require any adverse events or outcomes to be reported to the IRB.

Reporting

Maintaining FWA and the PU-IRB Registration

The HPA maintains the FWA and IRB registrations for the PU-IRB and notifies OHRP of any changes in the FWA or IRB membership as they occur.

HPA staff maintains a list of the IRB members (IRB rosters) that include the following information:
1. The information required by 45 CFR 46.103(b)(3) and 21 CFR 56.115(a)(5), which includes a list of IRB members identified by name; earned degrees; representative capacity; indications of experience such as board certifications, licenses, etc., sufficient to describe each member's chief anticipated contributions to IRB deliberations; and any employment or other relationship between each member and the institution; for
example: full-time employee, part-time employee, member of governing panel or board, stockholder, paid or unpaid consultant.
2. Whether the member is a primary member or alternate member.
3. The primary members whom each alternate member could substitute.

IRB Determinations Requiring Reporting
The following outlines the procedure for reporting to the appropriate institutional departments and offices, the institutional official, sponsors, and/or the appropriate regulatory agencies of events determined by the IRB to be:

1. Suspensions or termination based on serious or continuing non-compliance of IRB-approval of research,
2. Serious or continuing non-compliance, or
3. Unanticipated problems involving risks to subjects or others.

Following an IRB determination of any of the above, the HPA staff in collaboration with the IRB Chair prepares a letter for signature by the IRB Chair that contains the following information:

1. The nature of the event (whether or not the event was an unanticipated problem involving risks to subjects or others, serious or continuing non-compliance, or a suspension or termination of approval of research or a combination of these events),
2. The name of the institution conducting the research,
3. The title of the research project and/or grant proposal in which the problem occurred,
4. The name of the principal investigator on the protocol,
5. The assurance number assigned to the research project
6. A short summary of the project,
7. A detailed description of the problem including the findings of the organization and the reasons for the IRB’s decision,
8. Actions the institution is taking or plans to take to address the problem (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, increase IRB monitoring of the project),
9. Plans, if any, for any follow-up action.

The HPA staff sends a copy of this letter no more than one month following the review and final determination by the convened IRB to:

Institutional Entities:
1. Provost
2. Principal Investigator

Federal Agencies:
1. OHRP, if the study is subject to DHHS regulations or subject to a DHHS Federalwide Assurance.
2. FDA, if the study is subject to FDA regulations (21 CFR 50 and 56)
3. OHRP or the head of the agency as required by the agency, if the study is conducted or funded by any Federal Agency other than DHHS that is subject to the “Common Rule.”

Reporting to a regulatory agency does not occur if the event occurred at a site that was not subject to the direct oversight of the organization, and the agency has been notified of the event by the investigator, sponsor, another organization, or other mechanisms.

The HPA can provide copies to others as deemed appropriate by the Institutional Official.

6. Institutional Responsibilities

Administrative Support - HPA

The Human Protections Administrator, reporting to the Provost, has been established to support the IRB process. The HPA:

1. Assists the PU-IRB in preparing for and monitoring IRB meetings;
2. Maintains records on all human subjects research (including copies of all correspondence between the IRB and investigators) that takes place at PU;
3. Maintains databases for tracking studies;
4. Assists with preparation of meeting minutes;
5. Maintains files of minutes of full Board meetings;
6. Screens research applications for completeness and/or exemption prior to initiating the IRB review process;
7. Acts as a resource for investigators on general regulatory information, guidance with forms, and assistance in preparing an application for IRB review;
8. Maintains the institution’s Federalwide Assurance
9. Maintains a current list of the IRB members identified by name, earned degrees, representative capacity, indications of experience such as board certification or licenses sufficient to describe each member’s chief anticipated contributions to IRB deliberations, and any employment or other relationship between each member of the institution (e.g., full-time employee, board member)
10. Provides staff support to the IRB for all written correspondence;
11. Sends notices of approval, study closure, acknowledgements, etc.;
12. Generates and sends reminder notices to investigators of upcoming continuing reviews;
13. Maintains information on federal regulations relating to human subjects research;
14. Provides education regarding the IRB process and regulations to the Parker community.
Resources

PU provides adequate personnel, facilities and equipment to support the operation of the PU-IRB and HPA in performing the functions described in this document. PU provides necessary personnel and meeting space to perform the functions required by the IRB. It provides a research education and training program and methods for tracking training. Engagement of legal counsel is available, as appropriate. The Provost’s office, in conjunction with the HPA, manages conflicts of interest. The HPA has created, and bi-annually reviews, IRB Standard Operating Procedures. PU will maintain a Federalwide Assurance with the OHRP and provides open channels of communication for any issues related to the ethical conduct of research at Parker.

PU-IRB Member Training

There is an on-going education program for PU-IRB members that includes both initial and continuing education. The education focuses on the ethical principles and the regulatory requirements underpinning human subject protections and how to apply those to the initial and continuing review of research protocols.

All PU-IRB members and alternates complete IRB orientation before they may review research protocols and vote with the IRB. The initial orientation includes education on the following:

- History of human subject protections
- Ethical principles and The Belmont Report
- Regulatory requirements (DHHS regulations 45 CFR 46 and FDA Human Subject Regulations including, but not limited, to 21 CFR 50 and 56)
- Applicable Texas state law
- IRB’s role and responsibilities
- Application of the principles and regulations to the initial and continuing review of research
- Research protocol review criteria and review process
- Informed consent process and documentation
- Vulnerable populations: pregnant women, fetuses, prisoners, children and others
- Investigator responsibilities

Continuing education may be provided to the PU-IRB members throughout the year at IRB meetings. The HPA prepares presentations that highlight important IRB review responsibilities, new OHRP or FDA guidance on IRB topics, changes in federal or state and local regulations (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe) that relate to research and/or current topics that have ethical implications for IRB review.
Compensation of PU-IRB Members

PU provides no compensation to members of the PU-IRB.

Member Liability

PU-IRB members function as employees and agents of PU. As such, when acting in accordance with the PU-IRB Standard Operating Procedures, their actions are covered by PU general liability coverage.

7. Initial Review of a Research Study Involving Human Participants

Submission of Applications

All applications for review are submitted to the HPA. Applications are initially screened by the HPA for completeness and/or exemption before review by the IRB Chair and Vice-Chair. A complete new study submission for IRB review includes the following items as applicable:

1. PU-IRB New Study Application form,
2. Written study protocol,
3. Proposed informed consent document(s) or other consenting materials,
4. HIPAA consent (can be included in the informed consent document)
5. Recruitment materials (including direct advertising materials),
6. Survey instruments,
7. Investigator’s brochure, as applicable,
8. Other materials specific to the proposed study (e.g., sponsor correspondence with a regulatory agency such as the FDA regarding test item risk, etc.),
9. Waiver applications, as applicable.

If the application is incomplete or otherwise not fully prepared for review, a request is made for necessary changes or to provide additional information. HPA staff contact the investigator or members of the research team requesting clarification of protocol issues or revisions in the application and/or associated document(s) prior to referral to the IRB.

Once a complete packet of information has been received, it is assigned an ID assurance number. These unique numbers remain with the study and are never reassigned to a different study.

Determination of Type of Review

The HPA, IRB Chair or IRB member designee reviewer reviews the entire application and makes a determination as to whether the project constitutes human subjects research and, if so, the type of review (full Board review, expedited review, or exempt). All applications are
assigned to full Board review unless they meet the criteria for expedited review or the information submitted has been previously approved with modifications required by the full IRB. All projects involving the use of investigational drugs, devices, or biologics for which an IND/IDE is required receive full board review. If the IRB Chair or his/her IRB member designee determines that a study that meets the criteria for expedited review is more than minimal risk, the rationale for this decision must be documented. Studies that have been determined to be greater than minimal risk must receive full Board review.

**Determination of Research**

Federal regulations give the IRB the authority to oversee research involving human subjects. The IRB has no regulatory authority to oversee activities that are legitimately classified as something other than research. The purpose of this section is to describe how the HPA, in conjunction with the IRB, decides when it is acceptable to classify a project as a non-research activity. A project must be both research and involve human subjects to require PU-IRB review. It is the policy of PU that all projects be brought to the HPA so that a determination can be made as to whether the project requires IRB review. It is in the best interest of both the organization and the project leader to seek this determination before beginning a project in order to alleviate delays at the end of the project if publication is of interest.

In order for an activity to be research, it must have both elements of the DHHS definition of research:

1. the activity must be a systematic investigation
2. the primary goal of the activity must be to develop or contribute to generalizable knowledge

An activity that has only one of these properties is not research and will not be handled as such by the PU-IRB.

Prior to beginning a project at Parker, the HPA will make a determination as to whether the project is considered human subjects research. The following process is used:

1. Once a determination is made, the project leader will be informed and a letter of determination will be made available within the project package in IRBNet.
2. If it is determined the project meets the definition of human subjects research and requires IRB review, a complete New Study Application must be completed and added to the project package.
3. If it is determined that the project is not research, a “Not Research” letter will be provided to the project leader via IRBNet and no further action with the PU-IRB is required.

**Exempt Human Subjects Research**

Federal regulations recognize certain types of human subjects research as being exempt from
IRB oversight. PU policy requires that all human subjects research be reviewed by the IRB. Research meeting the “exempt” criteria provided in federal regulations is confirmed by the HPA, PU-IRB Chair, or his/her IRB member designee, based on review and approval of a New Study Application. Investigators are required to submit a New Study Application for review of exemption. A letter will be generated informing the investigator of approval or disapproval of the exemption, based on a consideration of the federal exemption categories.

The HPA, IRB Chair or his/her IRB member designee has the ultimate responsibility for making the decision whether the project meets the exempt criteria (see below). In making this determination, the HPA, Chair or his/her IRB member designee also considers any ethical issues including the possibility of coercion. When the HPA, Chair or his/her IRB member designee determines that the project does not qualify for exempt status, the application is considered for expedited review. If the study does not meet the criteria for expedited review it is referred for full Board review.

DHHS Exempt Criteria: Unless otherwise required by law or by department or agency heads, exemptions under DHHS regulations are limited to research activities in which the only involvement of human subjects will be in one or more of the following categories.

1. Research, conducted in established or commonly accepted educational settings, that specifically involve normal educational practices that are not likely to adversely impact students’ opportunity to learn required educational content or the assessment of educators who provide instruction. This includes most research on regular and special education instructional strategies, and research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

2. Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) if at least one of the following criteria is met:

   a. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

   b. Any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; or

   c. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7) that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.
3. Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and at least one of the following criteria is met:

   a. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained, directly or through identifiers linked to the subjects;

   b. Any disclosure of the human subjects’ responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation; or

   c. The information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and an IRB conducts a limited IRB review to make the determination required by 45 CFR 46.111(a)(7) that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.

For the purpose of this exemption category (3), benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing. Provided all such criteria are met, examples of such benign behavioral interventions would include having the subjects play an online game, having them solve puzzles under various noise conditions, or having them decide how to allocate a nominal amount of received cash between themselves and someone else.

If the research involves deceiving the subjects regarding the nature or purposes of the research, this exemption category is not applicable unless the subject authorizes the deception through a prospective agreement to participate in research in circumstances in which the subject is informed that he or she will be unaware of or misled regarding the nature or purposes of the research.

4. Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

   a. The identifiable private information or identifiable biospecimens are publicly available;

   b. Information, which may include information about biospecimens, is recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator
does not contact the subjects, and the investigator will not re-identify subjects;

c. The research involves only information collection and analysis involving the investigator’s use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for the purposes of “health care operations” or “research” as those terms are defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b); or

d. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

5. Research and demonstration projects that are conducted or supported by a Federal department or agency, or otherwise subject to the approval of department or agency heads (or the approval of the heads of bureaus or other subordinate agencies that have been delegated authority to conduct the research and demonstration projects), and that are designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including procedures for obtaining benefits or services under those programs, possible changes in or alternatives to those programs or procedures, or possible changes in methods or levels of payment for benefits or services under those programs. Such projects include, but are not limited to, internal studies by Federal employees, and studies under contracts or consulting arrangements, cooperative agreements, or grants. Exempt projects also include waivers of otherwise mandatory requirements using authorities such as sections 1115 and 1115A of the Social Security Act, as amended.

   a. Each Federal department or agency conducting or supporting the research and demonstration projects must establish, on a publicly accessible Federal Web site or in such other manner as the department or agency head may determine, a list of the research and demonstration projects that the Federal department or agency conducts or supports under this provision. The research or demonstration project must be published on this list prior to commencing the research involving human subjects.

6. Taste and food quality evaluation and consumer acceptance studies:

   a. If wholesome foods without additives are consumed, or

   b. If a food is consumed that contains a food ingredient at or below the level and for a
use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

7. **Storage or maintenance for secondary research for which broad consent is required:** Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use if an IRB conducts a limited IRB review and makes the determinations required by 45 CFR 46.111(a)(8).

8. **Secondary research for which broad consent is required:** Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met:
   
a. Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with 45 CFR 46.116(a)(1) through (4), (a)(6), and (d);

b. Documentation of informed consent or waiver of documentation of consent was obtained in accordance with 45 CFR 46.117;

c. An IRB conducts a limited IRB review and makes the determination required by 45 CFR 46.111(a)(7) and makes the determination that the research to be conducted is within the scope of the broad consent referenced in paragraph 8(a) of this section; and

d. The investigator does not include returning individual research results to subjects as part of the study plan. This provision does not prevent an investigator from abiding by any legal requirements to return individual research results.

Application of the exemption categories to research subject to the requirements of 45 CFR part 46, subparts B, C, and D, is as follows:

1. **Subpart B (Pregnant Women, Human Fetuses and Neonates).** Each of the exemptions at this section may be applied to research subject to subpart B if the conditions of the exemption are met.

2. **Subpart C (Prisoners).** The exemptions at this section do not apply to research subject to subpart C, except for research aimed at involving a broader subject population that only incidentally includes prisoners.

3. **Subpart D (Children).** The exemption categories 1, 4, 5, 6, 7 and 8 of this section may be applied to research subject to subpart D if the conditions of the exemption are met. Category 2(a) and 2(b) of this section only may apply to research subject to subpart D.
involving educational tests or the observation of public behavior when the investigator(s) do not participate in the activities being observed. Category 2(c) of this section may not be applied to research subject to subpart D.

FDA Exempt Criteria: Unless at least one of the following criteria is true, clinical investigations involving human participants are subject to IRB review under FDA regulations. The FDA exemption criteria are as follows:

1. Any investigation which commenced before July 27, 1981 and was subject to requirements for IRB review under FDA regulations before that date, provided that the investigation remains subject to review of an IRB which meets the FDA requirements in effect before July 27, 1981.

2. Any investigation commenced before July 27, 1981 and was not otherwise subject to requirements for IRB review under Food and Drug Administration regulations before that date.

3. Emergency use of a test article (see Definitions), provided that such emergency use is reported to the IRB within 5 working days. Any subsequent use of the test article at the institution is subject to IRB review. (see Section 21: Research Using FDA Regulated Products regarding Emergency use)

4. Taste and food quality evaluations and consumer acceptance studies, if wholesome foods without additives are consumed or if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural, chemical, or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.

When both DHHS and FDA regulations apply to research involving human subjects, the PU-IRB applies the most restrictive regulations from each to the research being conducted to ensure the protection of the rights and welfare of the human participants.

The decision charts (charts 2-7) below are utilized for determinations of exemptions. They are available at: [http://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html](http://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html)
Chart 2: Is the Research Involving Human Subjects Eligible for Exemption Under 45 CFR 46.101(b)?

Has HHS prohibited exemption of the human subjects research? (All research involving prisoners, some research involving children.)
[Footnote 1 to 45 CFR 46.101(i), 45 CFR 46.401(b)]

**"Only"** means that no non-exempt activities are involved. Research that includes exempt and non-exempt activities is not exempt.

NO

Will the only** involvement of human subjects be in one or more of the following categories?

Research conducted in established or commonly accepted educational settings, involving normal education practices?

AND/OR

Research involving the use of educational tests, survey procedures, interview procedures, or observation of public behavior?

YES

Exemption 45 CFR 46.101(b)(1) may apply.

Go to Chart 3

YES

Go to Chart 4

EXEMPTION 45 CFR 46.101(b)(2) OR (b)(3) MAY APPLY.

YES

Exemption 45 CFR 46.101(b)(4) may apply.

Go to Chart 5

YES

Exemption 45 CFR 46.101(b)(5) may apply.

Go to Chart 6

YES

Exemption 45 CFR 46.101(b)(6) may apply.

Go to Chart 7

NO

No exemptions to 45 CFR part 46 apply. Provisions of 45 CFR subpart A apply, and subparts B, C and D also apply if subjects are from covered vulnerable populations.

Go to Chart 8
Chart 3: Does Exemption 45 CFR 46.101(b)(1) (for Educational Settings) Apply?

From Chart 2

Is the research only conducted in established or commonly accepted educational settings? (Including but not limited to schools and colleges. May include other sites where educational activities regularly occur.)

NO

Research is not exempt under 45 CFR 46.101(b)(1).

Go to Chart 8

YES

Does the research study involve only normal education practices? (Such as research on regular and special education instructional strategies, or research on effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.)

NO

YES

Research is exempt under 45 CFR 46.101(b)(1) from all 45 CFR part 46 requirements.
Chart 4: Does Exemption 45 CFR 46.101(b)(2) or (b)(3) (for Tests, Surveys, Interviews, Public Behavior Observation) Apply?

1. **From Chart 2**
   - **Does the research involve only the use of educational tests, survey procedures, interview procedures, or observation of public behavior?**
     - **YES**
     - Does the research involve children to whom 45 CFR part 46, subpart D applies?
       - **YES**
         - Is the information obtained recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and could any disclosure of the human subjects’ responses outside the research reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, or reputation?
           - **YES**
             - Research is not exempt under 45 CFR 46.101(b)(2).
               - However, the 45 CFR 46.101(b)(3) exemption might apply.
             - Are the human subjects elected or appointed public officials or candidates for public office? (Applies to senior officials, such as mayor or school superintendent, rather than a police officer or teacher.)
               - **NO**
                 - Does any Federal statute require without exception that the confidentiality of personally identifiable information will be maintained throughout the research and thereafter?
                   - **NO**
                     - Research is not exempt under 45 CFR 46.101(b)(2) or (b)(3).
                       - Go to Chart 8
                   - **YES**
                     - Research is exempt under 45 CFR 46.101(b)(3) from all 45 CFR part 46 requirements.
               - **YES**
                 - Research is exempt under 45 CFR 46.101(b)(2) exemption from 45 CFR part 46 requirements.
           - **NO**
             - Does the research involve survey procedures, interview procedures, or observation of public behavior where the investigator participates in the activities being observed? [45 CFR 46.401(b)]
               - **YES**
                 - Research is not exempt under 45 CFR 46.101(b)(2) or (b)(3).
               - **NO**
                 - Are the human subjects elected or appointed public officials or candidates for public office? (Applies to senior officials, such as mayor or school superintendent, rather than a police officer or teacher.)
                   - **NO**
                     - Does any Federal statute require without exception that the confidentiality of personally identifiable information will be maintained throughout the research and thereafter?
                       - **NO**
                         - Research is not exempt under 45 CFR 46.101(b)(2) or (b)(3).
                       - Go to Chart 8
                       - **YES**
                         - Research is exempt under 45 CFR 46.101(b)(3) from all 45 CFR part 46 requirements.
             - **NO**
               - **NO**
                 - Research is not exempt under 45 CFR 46.101(b)(2) or (b)(3).

September 24, 2004
Chart 5: Does Exemption 45 CFR 46.101(b)(4) (for Existing Data Documents and Specimens) Apply?

From Chart 2

Does the research involve only the collection or study of *existing* data, documents, records, pathological specimens, or diagnostic specimens? *
("Existing" means existing before the research is proposed to an institutional official or the IRB to determine whether the research is exempt.)

YES

Are these sources **publicly available**?

YES

Research is exempt under 45 CFR 46.101(b)(4) from all 45 CFR part 46 requirements.

NO

NO

Will information be **recorded by the investigator** in such a manner that the subjects **cannot be identified**, directly or through identifiers linked to the subjects?

YES

Research is not exempt under 45 CFR 46.101(b)(4) from 45 CFR part 46 requirements.

NO

Go to Chart 8

* Note: See OHRP guidance on research use of stored data or tissues and on stem cells at http://www.hhs.gov/ohrp/policy/index.html#tissues and #stem, and on coded data or specimens at #coded for further information on those topics.

September 24, 2004
Chart 6: Does Exemption 45 CFR 46.101(b)(5) (for Public Benefit or Service Programs) Apply?

From Chart 2

Is the research or demonstration project conducted or approved by the Department or Agency Head?

YES

Does the research or demonstration project involve only the study, evaluation, or examination of:

Public benefit or service programs;

YES

Procedures for obtaining benefits or services under public benefit or service programs;

YES

Research is exempt under 45 CFR 46.101(b)(5) from all 45 CFR part 46 requirements.*

NO

Procedures for obtaining benefits or services under public benefit or service programs;

NO

Possible changes in or alternatives to public benefit or service programs or to procedures for obtaining benefits or services under public benefit or service programs;

YES

Possible changes in methods or levels of payment for benefits or services under those public benefit or service programs?

NO

Research is not exempt under 45 CFR 46.101(b)(5).

NO

Go to Chart 8

* Note: See OHRP guidance on exemptions at http://www.hhs.gov/ohrp/policy/index.htm#exempt for further description of requirements for this exemption.

September 24, 2004
Chart 7: Does Exemption 45 CFR 46.101(b)(6) (for Food Taste and Acceptance Studies) Apply?

From Chart 2

Does the research involve only a taste and food quality evaluation or a food consumer acceptance study?

YES

Are wholesome foods without additives consumed?

YES

Research is exempt under 45 CFR 46.101(b)(6) from all 45 CFR part 46 requirements.

NO

Is food consumed that contains a food ingredient, agricultural chemical, or environmental contaminant at or below the level found to be safe by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture?

YES

NO

Research is not exempt under 45 CFR 46.101(b)(6).

Go to Chart 8
**Limited IRB Review**

Research that qualifies for exemption that requires limited IRB review includes:

- **2(c)** - Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recording) and the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects.

- **3(c)** - Research involving benign behavioral interventions in conjunction with the collection of information from an adult subject through verbal or written responses (including data entry) or audiovisual recording if the subject prospectively agrees to the intervention and information collection and the information obtained is recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects.

- **7** - Storage or maintenance for secondary research for which broad consent is required: Storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research use.

- **8** - Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use if the criteria stated in the “Exempt Human Subjects Research” section are met.

**NOTE** – The Parker IRB is not presently allowing the use of broad consent and, therefore, the limited IRB procedures will not be applied to exemption categories 7 and 8 listed above.

The Parker IRB may use expedited review procedures to review research for which limited IRB review is a condition of exemption. Therefore, the HPA, IRB Chair or his/her IRB member designee will review studies meeting exemption categories 2(c) and 3(c).

Limited IRB review will include determining that there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data [45 CFR 46.111(a)(7)].

**Expedited Review**

The IRB expedited review process may be used in accordance with federal regulations for applications that qualify for expedited review. The PU-IRB Chair or his/her IRB member designee are responsible for these reviews. The criteria for approval using the expedited procedure are the same as those for review by a convened IRB.
The Chair or his/her IRB member designee may approve projects as submitted or require modifications prior to approval. They are not empowered to disapprove projects reviewed through the expedited process; in such cases, the application must be submitted for full Board review. If the IRB Chair or his/her IRB member designee determines that a new study that meets the criteria for expedited review is more than minimal risk, the rationale for this decision must be documented. Studies that have been determined to be greater than minimal risk must receive full Board review.

The PU-IRB members are notified on a meeting by meeting basis of all protocols that have been reviewed and approved through an expedited process. These reports include initial reviews, continuing reviews and reviews of modifications to previously approved research.

**Categories of Research That May be Approved Through Expedited Procedures**

The expedited review process may be used for the initial review of projects involving no more than minimal risk and fit one or more of the categories for expedited review procedures, as specified in the regulations [45 CFR 46.110, 21 CFR 56.110].

Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

In order to be reviewed and approved under expedited review procedures, the research must pose no more than minimal risk to subjects as determined by the IRB Chair or IRB member designee and must meet the criteria in one of the categories below.

1. Research on drugs for which an investigational new drug application [21 CFR 312] is not required or research on medical devices for which a) an investigational device exemption application (21 CFR Part 812) is not required or b) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

2. Collection of blood samples by finger stick, heel stick, ear stick or venipuncture as follows:

3. (a) from healthy, non-pregnant adults, who weigh at least 110 pounds. For these subjects, amounts drawn may not exceed 550 ml in an 8 weeks period and no more than 2 times per week; or

4. (b) from other adults and children, considering the age, weight, and health of the subjects, the collection procedure, the amount of blood to be collected, and the frequency with which it will be collected. For these subjects, the amount drawn may not exceed the lesser of 50 ml or 3 ml/kg in an 8-week period and collection may not occur more frequently than 2 times per week.
3. Prospective collection of biological specimens for research purposes by noninvasive means. Examples: (a) hair and nail clippings in a nondisfiguring manner; (b) deciduous teeth at the time of exfoliation or if routine patient care indicates a need for extraction; (c) permanent teeth if routine patient care indicates a need for extraction; (d) excreta and external secretions (including sweat); (e) uncannulated saliva collected either in an unstimulated fashion or stimulated by chewing gumbase or wax or by applying a dilute citric solution to the tongue; (f) placenta removed at delivery; (g) amniotic fluid obtained at the time of rupture of the membrane prior to or during labor; (h) supra- and subgingival dental plaque and calculus, provided the collection procedure is not more invasive than routine prophylactic scaling of the teeth and the process is accomplished in accordance with accepted prophylactic techniques; (i) mucosal and skin cells collected by buccal scraping or swab, skin swab, or mouth washings; (j) sputum collected after saline mist nebulization.

4. Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.) Examples: (a) physical sensors that are applied either to the surface of the body or at a distance and do not involve input of significant amounts of energy into the subject or an invasion of the subject's privacy; (b) weighing or testing sensory acuity; (c) magnetic resonance imaging; (d) electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, oto- and retinography, ultrasound, diagnostic infrared imaging, doppler blood flow, and echocardiography; (e) moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual.

5. Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for non-research purposes (such as medical treatment or diagnosis).

6. Collection of data from voice, video, digital, or image recordings made for research purposes.

7. Research on individual or group characteristics or behavior (including, but not limited to, research on perception, cognition, motivation, identity, language, communication, cultural beliefs or practices, and social behavior) or research employing survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

The OHRP decision chart (chart 8) below is utilized for determinations of expedited review. It is available at: http://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html
Chart 8: May the IRB Review Be Done by Expedited Procedures Under 45 CFR 46.110?*

* Note: See expedited review categories and OHRP guidance on the use of expedited review procedures at http://www.hhs.gov/ohrp/policy/index.html#expedited for further information on expedited review.

From Chart 2, 3, 4, 5, 6, or 7

Has the research been *previously reviewed* and approved by the IRB?

YES

Is the review a *continuing review*?

[45 CFR 46.109(d)]

NO

Does the research present *no more than minimal risk* to human subjects *and* does the research involve *only procedures included in categories 1 through 7* on the list of categories of research that may be reviewed through an expedited review procedure?

[45 CFR 46.110(b)(1)]

YES

Is the research *classified*?

[Paragraph (D) of Categories of Research That May Be Reviewed By an IRB through an Expedited Review Procedure.]

NO

Could identification of subjects put them at risk of criminal or civil liability, or be socially or economically damaging?

[Paragraph (C) of Categories.]

YES

Research is eligible for IRB review through expedited procedures. Agency head may restrict, suspend, terminate or choose not to authorize an institution’s or IRB’s use of the expedited review procedure. [45 CFR 46.110(d)]

NO

Are measures in place to make risks no more than minimal?

YES

Go to Chart 10

NO

Does the review involve a *minor change* in approved research during the (one year or less) period of approval?

[45 CFR 46.110(b)(2)]

NO

Review by convened IRB is required.

YES

Go to Chart 9

September 24, 2004
Scope of Review

After initial review of applications by the HPA for completeness, the PU-IRB convened or expedited review of applications is conducted to:

1. Consider the scientific or scholarly design to determine that the use of human subjects is relevant and appropriate to answer the questions being asked;
2. Consider ethical issues with regard to the study’s design and conduct;
3. Determine that the proposed recruitment and enrollment plan, including the inclusion and exclusion criteria used, afford selection of subjects from the population that is equitable given the potential benefits and risks of the research;
4. Identify the risks associated with the research, as distinguished from the risks of therapies the subjects would receive even if not participating in research;
5. Identify level of risk;
6. Determine that the risks are minimized to the extent possible by using procedures consistent with sound research design and which do not unnecessarily expose subjects to risks, and whenever appropriate, by using procedures already being performed on subjects for non-research diagnostic or treatment purposes;
7. Identify the probable benefits to be derived from the research;
8. Determine that the risks are reasonable in relation to the anticipated benefits to subjects, if any, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (e.g. the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.;
9. Assure that potential subjects are provided with an accurate and fair description of the risks or discomforts and the anticipated benefits;
10. Require informed consent be sought and documented from each prospective subject or their legally authorized representative, or determine to waive these requirements according to appropriate regulatory requirements;
11. Determine intervals of periodic review;
12. Determine that adequate plans are in place for data and safety monitoring, where appropriate;
13. Determine the adequacy of the provisions to protect the privacy of subjects and to maintain the confidentiality of the data;
14. Where the subjects are likely to be members of a vulnerable population, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons determine that appropriate additional safeguards are in place to protect the rights and welfare of these subjects.
Primary Reviewer Process

The IRB Chair, or his/her IRB member designee, may assign a Primary Reviewer in advance of a full Board meeting for new study applications. The Chair may, at his/her discretion, serve as the Primary Reviewer. In selecting the Primary Reviewer, consideration is given to the individual’s knowledge of the subject area embodied in the proposal. If, in the opinion of the IRB Chair, the IRB membership for a scheduled meeting does not include someone with the relevant scientific or scholarly expertise to conduct an appropriate review of a particular protocol, the Chair may take any of the following actions: 1) re-assign the particular protocol to another meeting where an IRB member with appropriate expertise will be in attendance and can act as the Primary Reviewer, or 2) invite a consultant with the appropriate expertise to attend the meeting. If the IRB chair chooses to invite a consultant to be the Primary Reviewer, the consultant would act under the procedures for consultants as described in the Use of Consultants section.

For new projects, the Primary Reviewer reviews the application, the proposed informed consent document(s) and assent documents, recruitment materials (including direct advertising materials), the study protocol, and if applicable the investigator’s brochure. A New Study Application Primary Reviewer Checklist has been developed to assist the Primary Reviewer with review of new study applications.

The Primary Reviewer may request additional information from the investigator via the HPA in advance of the Board meeting. The Primary Reviewer leads the discussion of the application under review. The Primary Reviewer may not have a conflict of interest regarding the study under review and is expected to notify the Chair of any conflict.

Use of Consultants

At the time of preliminary review of a project application, the PU-IRB Chair or Primary Reviewer may determine that the study requires further review by a consultant with expertise outside of the current PU-IRB membership. This determination may be made based on the scientific design of the study, the ethical issues of the study, the potential risks or benefits of the study, specific privacy and confidentiality concerns, or considerations relative to a particular study population.

Upon identifying the need for a consultant review, the Chair and/or Primary Reviewer in consultation with the Chair will identify a consultant based on the particular issues to be addressed. The Chair will determine that the consultant does not have a conflict of interest. The consultant will not have IRB voting privileges.

Revisions Prior to Final Approval

Revisions to human subjects applications may be required by the PU-IRB. Correspondence is sent to the investigator detailing requests for revisions, clarification, or additional information as
well as information regarding continuing review. The investigator has a designated time period, not to exceed 60 days, in which to respond to the revisions requested. If the investigator does not respond in the designated time period, the application may be withdrawn by the PU-IRB with notification sent to the investigator. If the investigator wishes to conduct a study that has been withdrawn, s/he must submit a new application, incorporating comments from the prior PU-IRB review.

When specific changes are requested by the convened IRB in the protocol and/or consent document(s) (i.e., changes requiring no more than simple concurrence), these are reviewed for compliance by the IRB Chair or designee before final approval is given (if allowed by the convened PU-IRB at the time of the IRB motion). In instances where extensive or substantive clarifications or modifications are requested during a full Board review, the application is deferred and the revised documents are returned to the full Board for its review and approval. The application receives final approval when all required changes have been submitted and approved.

For the purposes of determining the expiration date the date of approval is the date of the convened IRB meeting at which the application was reviewed and modifications were requested.

**Final Approval**

Upon receipt of final approval, IRB approved materials will be available via IRBNet. These materials may include stamped approved informed consent document(s) and other materials (e.g., letters to subjects, ads) with the PU-IRB date of approval and the date of expiration. IRB stamped materials should be used during the implementation of the study. The principal investigator (PI) and designated members of the research team will be notified of the approval and allowed access to currently approved documents.

**Appeal of PU-IRB Decisions**

Investigators may appeal PU-IRB requirements for specific changes in the protocol and/or consent document(s). If the application is being reviewed under expedited procedures, the IRB Chair works directly with the investigator to resolve outstanding issues. If the IRB Chair and investigator cannot resolve the issue(s), the project is referred to full Board for review.

If the full Board decides to require specific changes or to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision. An investigator may appeal any of the requested changes or the disapproval. Such appeals are submitted in writing via IRBNet as a response to the meeting minutes and disapproval letter. Such appeals must be reviewed at a full Board meeting. If the appeal requires discussion or explanation beyond what can be provided to the Board in written format, the investigator may be invited by the IRB Chair to attend the full Board meeting at which the appeal is presented. The investigator is invited for the purpose of answering questions and participating in discourse with Board members. The investigator leaves prior to the PU-IRB discussion and
vote on the issues.

In the case of a decision by the PU-IRB to disapprove, suspend, or terminate a project, the decision may not be reversed by other parties. Investigators have the right to appeal an IRB decision one time if they are able to provide new information, a revised protocol or clarification of information presented on the application for appeal. The appeal must be reviewed at a regularly scheduled meeting. The decision of the IRB on the appeal shall be final.

**Length of Approval**

Except for studies determined to be exempt from IRB oversight, all human subjects studies are subject to continuing review based on the level of risk as assessed by the Board. This review takes place at a minimum annually and may require more frequent review or reports as determined by the PU-IRB. For projects receiving full Board review, the length of approval is calculated from the date of the convened meeting at which the IRB approves the protocol or approves the research with modifications. The appropriate length of approval is considered as a part of the full Board discussion.

Projects requiring review more frequently than annually may include:

1. Experimental therapies in which the clear potential for significant adverse experiences have been identified at the time of review;

2. Non-therapeutic projects based on risk information provided at the time of initial review;

3. Projects in which new information provided during the duration of the study (including at the time of continuing review) indicates a high probability of significant adverse experiences not previously reported;

4. Projects in which local or outside adverse experience reports create new concerns regarding the need for closer project scrutiny; or

5. Projects where PU-IRB has concerns with regard to previous or potential serious or continuing noncompliance.

In such cases, approvals may be granted for time periods less than one year, or a limited number of subjects over a period not to exceed one year, or additional monitoring may be required.

For projects approved via the expedited process, the IRB Chair or his/her IRB member designee determines the length of approval, not to exceed one year. Investigators are notified in writing as to when their projects are due for continuing review.
8. Continuing Review of a Research Study

Unless the Parker IRB determines otherwise, the IRB will conduct continuing review of research requiring review by the convened IRB at intervals appropriate to the degree of risk, but not less than once per year, except in the following circumstances:

1. Research eligible for expedited review in accordance with federal regulations (45 CFR 46.110)
2. Research reviewed by the IRB in accordance with the limited IRB review process
3. Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB approved study:
   a) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
   b) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care

Records of continuing review activities, including the rationale for conducting continuing review of research that otherwise would not require continuing review as described above will be documented by the IRB.

When a research project is due for continuing review, the IRB Chair will inform the HPA, and the HPA emails the principal investigator (PI) and specified members of the research team notifying them of the upcoming final submission date for review. The first email is sent 60 days prior to the expiration date. Additional emails are sent at 30 days prior to the expiration date and on the expiration date. On the expiration date, notification is sent to the PI and all research team members indicating that PU-IRB approval has expired and no further research activity may occur on or after that date, except those related to patient safety as directed by the PU-IRB.

If the PI wishes to continue the project, the IRB should be notified as soon as possible to determine the appropriate process. Continuation of research interventions or interactions with already enrolled participants is allowed only when the IRB or IRB Chair determines that it is in the best interest of individual subjects to do so.

Applications for continuing review and associated materials are submitted electronically via IRBNet. The HPA staff conducts a preliminary review of applications for completeness. The HPA may return applications to the investigator for modifications. Applications that appear to be complete are forwarded to the IRB Chair or his/her IRB member designee for review and determination as to full Board review or expedited review.

All IRB members receive the Continuing Review Application form, study protocol, approved informed consent document(s) and assent document(s), HIPAA consent document, the
number of participants accrued, a status report on the progress of the research and other materials as outlined in the Continuing Review Application form.

All IRB members receive all materials via email. Members can review the complete electronic project history which includes the original study application, protocol(s), currently active modifications reviewed by the PU-IRB under expedited or full Board review, and reports of unanticipated problems and adverse event reports. All IRB members attending the meeting must review the materials in sufficient depth to discuss the information at the convened meeting.

The IRB or expedited reviewer reviews the consent document with the continuing review application particularly to ensure that the consent document remains accurate and complete. This is done by assessing the progress of the study and any changes to the risk/benefit ratio of the overall project. The PU-IRB may require changes to the consent document if they determine the changes will provide more accurate or complete information to the study subject.

Procedures for expedited or full Board review, criteria for approval, and revision prior to approval, are identical to those described above for Initial Reviews.

As part of the continuing review of research, the IRB or IRB chair may determine that a project needs verification from sources other than the investigators that no material changes have occurred since the previous IRB review. Projects requiring this verification may include:

1. Complex projects involving unusual levels or types of risks to subjects, or
2. Projects involving vulnerable populations, or
3. Projects conducted by an investigator who previously failed to comply with IRB determinations, or
4. Projects where the continuing review application or reports from other sources have indicated that changes may have occurred without IRB approval.

If the IRB or expedited reviewer determines that a project requires verification from other sources, they can send a PU-IRB monitor to review the study.

For projects undergoing continuing review, the IRB may approve, approve pending required actions on the part of the investigator, table, or disapprove the protocol. Investigators are notified in writing of the decision of the PU-IRB and any changes required. Final approval is not granted until all required changes have been made and submitted for review and approval. When final approval will likely not be given prior to the expiration date, the minutes for full Board reviews note the current expiration date and note that no further research may be conducted on or after that date. Likewise, for expedited review, when approval will not be given prior to the expiration date, the HPA notifies the PI of the current expiration date on or after which all research activity must be discontinued pending receipt of continuing review approval.

Upon receipt of final approval, stamped approved informed consent document(s) and other
materials (e.g., letters to subjects, ads) with the PU-IRB date of approval, and the date of expiration will be available within IRBNet. The system notifies the PI and designated members of the research team of the approval and allows access to currently approved documents. In addition, the investigator may access an electronic memo in IRBNet indicating the type of review, date of next continuing review, and a summary of investigator responsibilities. The memo reminds investigators that changes in research activity may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to subjects.

**Continuing Reviews That May be Reviewed and Approved Through Expedited Procedures**

The continuing review of research may be reviewed using expedited procedures in the following circumstances:

1. If continuing review of the research was previously approved by the convened IRB and conditions have changed to make the research eligible for expedited review under criteria 1 through 7 listed in the “Expedited Review” section of this policy (e.g., research is within those categories and experience confirms the research to be of no greater than minimal risk).

2. If continuing review of the research was previously approved by the convened IRB and
   a) The research is permanently closed to the enrollment of new subjects, and all subjects have completed all research-related interventions, and the research remains active only for long-term follow-up of subjects; or
   b) No subjects have been enrolled and no additional risks have been identified; or

3. [NOTE: Refers to expedited category 8 in the chart below and described in the OHRP Expedited Review Categories (1998)] If continuing review of the research was previously approved by the convened IRB and
   a) The research is not conducted under an investigational new drug application or an investigational device exemption, and
   b) The IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk, and
   c) No additional risks have been identified since IRB review at a convened meeting.
   [NOTE: Refers to expedited category 9 in the chart below and described in the OHRP Expedited Review Categories (1998)]

The OHRP decision chart (chart 9) below is utilized for determinations of continuing review by expedited procedures. It is available at: [http://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html](http://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html)
Chart 9: Can Continuing Review be Done by Expedited Procedures Under 45 CFR 46.110?

From Chart 8

Has the research been previously reviewed and approved by the IRB using expedited procedures?

YES

Have conditions changed such that the research is no longer eligible for expedited review (e.g., protocol change, or experience shows research to be of greater than minimal risk)?

YES

Review by convened IRB is required.

NO

Go to Chart 10

NO

Research is eligible for IRB review through expedited procedures.

YES

Has any additional risks been identified since IRB review at a convened meeting?

YES

Has the IRB determined and documented at a convened meeting that the research involves no greater than minimal risk?

YES

September 24, 2004

NO

CATEGORY 8

(a) For this site:
Is the research permanently closed to enrollment of new subjects? and
Have all subjects completed all research-related interventions? and
Does the research at this site remain active only for long-term follow-up of subjects?

YES

(b) Have no subjects been enrolled at this site? and Have no additional risks been identified anywhere?

NO

NO

CATEGORY 9

Is the research conducted under an IND or IDE?

NO

January 23, 2019

* Note: See expedited review categories, OHRP guidance on the use of expedited review procedures and on continuing review at http://www.hhs.gov/ohrpr/policy/index.html#expedited and #continuing for further information on expedited review.
9. Amendments to a Research Study

Investigators must report planned changes in the conduct of a study promptly to the IRB and receive approval from the PU-IRB prior to implementing these changes, except when necessary to eliminate apparent immediate hazards to the subject. The investigator is required to promptly notify the IRB of these instances using the Amendment Application form.

The approval documentation sent to investigators of exempt, expedited, and full Board studies notifies them of the need for submitting any changes in their research projects to the PU-IRB for review and approval, prior to implementation.

Modifications that need IRB approval include, but are not limited to, procedural changes to a protocol, adding or removing investigators, and changes in recruitment materials and informed consent document(s). Amendments are made by completing the Amendment Application and/or associated electronic documents. Changes are documented in the system so that reviewers can view tracked-change versions of materials.

The principal investigator cannot request that an amendment be considered as part of a continuing review application. The PU-IRB requires that continuing review must occur separately. The amendment and continuing review can be reviewed by the IRB on the same IRB meeting agenda.

All IRB members receive the study Amendment Application with the requested modifications identified, newly proposed consent document(s) and assent document(s), recruitment materials (if there are changes), other proposed correspondence with subjects (if applicable and the materials have changed), changed protocols or investigator brochures, and other materials as determined by the IRB Chair. All IRB members must review the materials in sufficient depth to discuss the information at the convened meeting. The IRB will determine if previously enrolled subjects are to be re-consented or otherwise notified of the amended protocol or research-related documents.

Investigators are notified of the decision of the PU-IRB and any changes required. Final approval is not granted until all required changes have been made and submitted for review and approval. Upon receipt of final approval, stamped approved informed consent document(s) and other materials (e.g., letters to subjects, ads) with the PU-IRB date of approval and the date of expiration will be available to the PI. The system notifies the PI and designated members of the research team of the approval and allows access to currently approved documents.
**Amendments to the Research That May be Reviewed and Approved Through Expedited Procedures**

Modifications to previously approved research projects may be expedited if the modification involves only a minor modification to the approved project during the (one year or less) period of approval.

A ‘minor change’ is defined in this policy as a change in the research plan that does not increase the risks or decrease the benefits related to the study (including risks related to procedures and methods, and to modifications that might negatively impact the statistical analysis of the research). If the change affects two of the following three aspects of the research, (i) the purpose, (ii) the population or (iii) the procedures; the change cannot be considered ‘minor’ and must be reviewed by the convened IRB unless the research itself is no greater than minimal risk and is limited to the categories of research eligible for expedited review.

**10. Closure of a Research Study**

The PI may close a study by submitting the PU-IRB Study Closure Report. The study may also be closed by the HPA/PU-IRB. Studies can be closed once all research participants have completed all research-related interventions, long-term follow-up and collection of identifiable information. Study closures may be expedited by the IRB Chair or his/her IRB member designee. However, the IRB Chair or his/her IRB member designee retains the right to request full IRB review of study closures, if necessary. The PI and designated members of the research team will be notified once the study closure has been approved, and a study closure letter will be available. Once the closure is accepted by the IRB, no additional research can be conducted related to that protocol other than data analysis.

**11. Suspension of a Research Study by Investigator, Sponsor or Responsible Agency**

If an investigator, sponsor, or responsible agency voluntarily suspends a protocol, the investigator must inform the PU-IRB by submitting a Study Suspension Report on which the details of the suspension should be provided. This Study Suspension Report will be reviewed by the IRB at a convened meeting. The study suspension is not considered to be a reportable event unless the IRB independently determines that suspension or termination has occurred because there was an unanticipated problem involving risks to subjects or others or there was an incident of serious or continuing non-compliance.

The IRB (or IRB Chair or IRB member designee when there are immediate serious safety issues) can take the following actions regarding study suspensions:
1. Suspend or terminate IRB approval of the research study
2. Suspend IRB approval for certain activities (e.g., recruitment, enrollment)
3. Administratively hold all other research by the same investigator

To reinstate a suspended research study, the investigator must submit an Amendment Application to the IRB. The application must restate the reason for the study suspension and outline changes in the study protocol, informed consent or other materials that appropriately address the factors leading to the suspension, if applicable. For study suspensions related to risk, the IRB will review the amendment to reinstate the study at a full Board meeting. For study suspensions unrelated to risk (e.g., low study drug supply), the IRB Chair or IRB member designee can approve the amendment to reinstate the study through expedited review.

In the event that a Study Amendment Application would need to be submitted at the same time as a Study Suspension Report, submitting the Study Amendment Application will suffice.

12. Reporting of Unanticipated Problems Involving Risks to Subjects and Others (UPIRSOs)

The PU-IRB is responsible for ongoing monitoring of the safety and welfare of human subjects. Part of this monitoring is on-going review and assessment of unanticipated problems involving risks to human subjects or others (UPIRSOs) related to participation in the research. Investigators are required by federal regulations and PU-IRB policies to promptly report to the PU-IRB all UPIRSOs. An unanticipated problem, in general, includes any incident, experience, or outcome that meets ALL of the following criteria:

- unexpected (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents, such as the IRB-approved research protocol and informed consent document; and (b) the characteristics of the subject population being studied;
- related or possibly related to participation in the research (for the PU-IRB, possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

Reporting is required of all UPIRSOs, including those which may occur after the participant has completed or is withdrawn from the study, or following study closure.

Expectations for Reporting Include:

- Any event or unanticipated problem occurring at a site for which the PU-IRB has direct oversight responsibility that meets all three criteria for an UPIRSO, and is therefore reportable.
• Any event or unanticipated problem occurring at a PU location, whether or not the PU-IRB has direct oversight responsibility, in which a determination has been made by the FDA, research sponsor, coordinating center, data safety monitoring board (DSMB)/data monitoring committee (DMC) or other centralized monitoring. An incident, experience, or outcome that meets the three criteria for an UPIRSO warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects or others.

• Any non-local event or unanticipated problem that has been determined to meet the definition of an UPIRSO by the monitoring entity. When non-local adverse events are received by the investigator, s/he should assess whether the monitoring entity has identified the adverse event as being an UPIRSO. Note – ONLY those non-local adverse events and unanticipated problems identified by the monitoring entity to meet the definition of an UPIRSO should be reported to the PU-IRB.

**Relationship Between Adverse Events and Unanticipated Problems**

The term adverse event in general is used to include any event meeting the following definition:

• Any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research (modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice).

**Which Adverse Events are Unanticipated Problems (UPIRSOs)?**

Only a small subset of adverse events occurring in human subjects participating in research will meet the criteria for prompt reporting as an unanticipated problem. The key question regarding a particular adverse event is whether it meets the three criteria for an UPIRSO. To determine whether an adverse event is an UPIRSO, the following questions should be asked:

• Is the adverse event **unexpected**?

• Is the adverse event **related or possibly related** to the research?

• Does the adverse event suggest a **greater risk of harm** than was previously known or recognized?

If the answer to all three questions is yes, then the adverse event is an unanticipated problem and must be reported to appropriate entities. The following diagram helps to explain the relationship between adverse events and unanticipated problems:
Assessing Whether an Adverse Event is Unexpected

An unexpected adverse event is defined as any adverse event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is not consistent with either:

1. The known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or

2. The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject’s predisposing risk factor profile for the adverse event.

(Modified from the definition of unexpected adverse drug experience in FDA regulations at 21 CFR 312.32(a).)

The vast majority of adverse events occurring in the context of research are expected in light of (1) the known side effects of the research procedures; (2) the expected natural progression of subjects’ underlying diseases, disorders, and conditions; and (3) subjects’ predisposing risk factor profiles for the adverse events. Thus, most individual adverse events do not meet the first criterion for an unanticipated problem and do not need to be reported under the HHS regulations 45 CFR part 46.103(a) and 46.103(b)(5) and the corresponding FDA regulations 21 CFR 56.108(b)(1), 21 CFR 312.53(c)(1)(vii), and 21 CFR 312.66.

Assessing Whether an Adverse Event is Related or Possibly Related to Participation in Research
Adverse events may be caused by one or more of the following:

1. The procedures involved in the research;
2. An underlying disease, disorder, or condition of the subject; or
3. Other circumstances unrelated to either the research or any underlying disease, disorder, or condition of the subject.

In general, adverse events that are determined to be at least partially caused by (1) would be considered related to participation in the research, whereas adverse events determined to be solely caused by (2) or (3) would be considered unrelated to participation in the research.

**Does an Adverse Event Place Subjects or Others at a Greater Risk of Harm than was Previously Known or Recognized?**

The first step in determining if the adverse event meets the third criteria of an UPIRSO is to determine whether the unanticipated problem is serious.

A serious adverse event is generally defined as any adverse event that:

1. Results in death;
2. Is life-threatening (places the subject at immediate risk of death from the event as it occurred);
3. Results in inpatient hospitalization or prolongation of existing hospitalization;
4. Results in a persistent or significant disability/incapacity;
5. Results in a congenital anomaly/birth defect; or
6. Based upon appropriate medical judgment, may jeopardize the subject’s health and may require medical or surgical intervention to prevent one of the other outcomes listed in this definition.

The PU-IRB considers adverse events that are unexpected, related or possibly related to participation in research, and serious to be the most important subset of adverse events representing unanticipated problems because such events always suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized and routinely warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects.

However, other adverse events that are unexpected and related or possibly related to participation in the research, but not serious, would also be unanticipated problems if they suggest that the research places subjects or others at a greater risk of physical or psychological harm than was previously known or recognized. Again, such events routinely warrant consideration of substantive changes in the research protocol or informed consent process/document or other corrective actions in order to protect the safety, welfare, or rights of subjects.
of subjects or others.

**Reportable Unanticipated Problems that are not Adverse Events**

Unanticipated problems are incidents or experiences that occur during the research and are not expected based on information about the study provided to the IRB. Similar to adverse events, not all unanticipated problems are research-related or result in real or potential additional risks to subjects or others. Unlike adverse events, which occur primarily in biomedical research, unanticipated problems occur in both biomedical and social or behavioral research. Upon becoming aware of any other incident, experience, or outcome that may represent an unanticipated problem, the investigator should assess whether the incident, experience, or outcome represents an unanticipated problem by applying the criteria for a UPIRSO as described above. If the investigator determines that the incident, experience, or outcome represents an unanticipated problem, the investigator must report it promptly to the IRB [45 CFR 46.103(b)(5)].

Unanticipated problems need not be adverse events to be considered UPIRSOs. Examples of unanticipated problems that are UPIRSOs, but not adverse events, are a breach of confidentiality, stolen laptop computer with identifiable study data, a research assistant suffers an injury from faulty research equipment, research assistant is accosted in the housing project where they are interviewing residents for a study, and a subject’s child accidentally takes a dose of the study medication without any harmful effects.

**Reportable Protocol Deviations**

Federal regulations require that the IRB reviews proposed changes in the research protocol and ensures that the investigator does not initiate the change prior to obtaining IRB approval. The only exception to this requirement is when it is necessary to make a change to eliminate apparent immediate harm to the subject [45 CFR 46.103 (b) (4) (iii), 21 CFR 56.108 (a) (4)]. Any changes to the research must be either prospectively approved or promptly reported to the IRB according to the federal regulations and PU-IRB policy and procedures. Therefore, all major protocol deviations meeting the definition of a UPIRSO must be promptly reported to the IRB by the PI once the violations are discovered.

When a protocol deviation occurs (i.e., a divergence from the protocol that adversely affects the rights, safety or welfare of the subjects, or which significantly adversely impact the integrity of research data) the PI will report such major deviations/violations on the UPIRSO Form. The PU-IRB Chair will review actions taken on such issues and act promptly if there are any issues or actions regarding compliance with human subject protection requirements and, if necessary, halt enrollment into a study.

**Adverse Event Reporting for Clinical Trials of Devices Under Investigational Device Exemptions**
Investigators are required to submit to the PU-IRB and the sponsor a report of any unanticipated adverse device effect (UADE) occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect [21CFR812.150(a)(1)]. An UADE also meets the definition of an UPIRSO and is defined as follows:

1. “any serious adverse effect on health or safety or any life-threatening problem or death caused by, associated with, a device, if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with the device that relates to the rights, safety, or welfare of subjects [21CFR812.3(s)].

Events That do not Require Reporting to the IRB

1. Local adverse event or problem that is expected or is not associated with a greater risk of harm to participant or others than previously known;
2. Non-local adverse event or problem that is expected or is not associated with a greater risk of harm to participant or others than previously known; and
3. Minor protocol violations.

Timeframe for Reporting

Events that meet the criteria for a UPIRSO and are also serious adverse events should be reported to the IRB within one (1) week of the investigator becoming aware of the event. Any other events that meet the criteria for a UPIRSO should be reported to the IRB within two (2) weeks of the investigator becoming aware of the problem.

If the report cannot be completed in its entirety within the required time period, a preliminary report should be submitted. The report should be amended once the event is resolved and/or more information becomes available.

At the time of continuing review, the IRB requests a summary of all local UPIRSOs, local adverse events and a report from the Data Safety Monitoring Board, if one exists. This is outlined on the Continuing Review Application form.

Content of Reports of UPIRSO submitted to the PU-IRB

Investigators must fill out the UPIRSO form to include the following information when reporting an adverse event or any other incident, experience or outcome as an UPIRSO to the IRB:

1. Appropriate identifying information for the research protocol, such as the title, investigator’s name, and the IRB assurance number;
2. A detailed description of the adverse event, incident, experience, or outcome;
3. An explanation of the basis for determining that the adverse event, incident, experience, or outcome represents a UPIRSO; and
4. A description of any changes to the protocol or other corrective actions that have been taken or are proposed in response to the UPIRSO.

**PU-IRB UPIRSO Review Process**

The IRB Chair or his/her IRB member designee will review all reports of unanticipated problems. If a reported event poses serious risk to subject safety, the Chair or IRB member designee may immediately suspend the study. In most cases, the IRB will review a corrective action plan provided by the PI to ensure resolution of the immediate scenario and prevent future occurrences.

Any unanticipated problem involving more than minimal risk(s) to participants or others will be reviewed by the convened IRB. For unanticipated problems referred to the convened IRB, all members will receive the UPIRSO form and informed consent form, where relevant, as well as any correspondence with the investigator to date. The convened IRB should make a final determination as to whether the event constitutes an UPIRSO.

The IRB has the authority to suspend or terminate IRB approval of protocols that are found to pose unanticipated or heightened risk. Other actions taken by the IRB may include but are not limited to:

1. Modification of the research protocol;
2. Modification of the information disclosed during the consent process;
3. Additional information provided to past participants;
4. Notification of current participants, which is required when such information might relate to participants’ willingness to continue to take part in the research;
5. Requirement that current participants re-consent to participation;
6. Modification of the continuing review schedule;
7. Monitoring of the research;
8. Monitoring of the consent;
9. Obtaining more information pending a final decision;
10. Referral to other organizational entities (e.g., President, Parker Board); and/or
11. Requirements for additional training for investigators and/or research staff.

The HPA is responsible for all required reporting of unanticipated problems involving risks to subjects or others and the resulting IRB actions to the appropriate federal agencies [45 CFR 46.103(b)(5)].

**13. Routine and For-Cause Audits**

The PU-IRB has the authority to perform routine and for-cause audits to evaluate compliance
with federal regulations, state and local laws (including tribal law passed by the official
governing body of an American Indian or Alaska Native tribe) and Parker Health System
Institutional Review Board Standard Operating Procedures. This includes the inspection of
research records and signed informed consent documents. The IRB may ask investigators to
provide written responses to questions from the IRB about the conduct of a study. The IRB
may request that a designated representative observe research activities, including the
process of informed consent.

14. Informed Consent and Documentation of Participation

Obtaining informed consent is a basic ethical obligation for researchers. The process of
consent should ensure that potential subjects are provided with information about the research
project that is understandable and permits the subject to make an informed and voluntary
decision about whether or not to participate.

An investigator should seek informed consent only under circumstances that provide the
prospective subject or the legally authorized representative (LAR) sufficient opportunity to
discuss and consider whether or not to participate and that minimize the possibility of
coercion or undue influence. The information that is given to the subject or the LAR must be
in language understandable to the subject or the LAR. The prospective subject or the LAR
must be provided with the information that a reasonable person would want to have in order
to make an informed decision about whether to participate, and an opportunity to discuss
that information.

While the initial process is prospective and takes place prior to any research activity, consent
should also be an ongoing educational interaction between the investigator and the research
subject that continues throughout the study.

The informed consent process is not an exercise in persuasion. If an investigator has a
relationship with potential subjects (physician-patient, instructor-student, employer-
employee), care should be taken to avoid recruitment methods that may be seen as
coercive due to the special relationship between parties.

Consent is a legal concept. Only legally competent adults can give legally effective informed
consent. Children and those individuals who are not competent to provide consent should be
given the opportunity to assent to participate in the research project. Assent is a
knowledgeable agreement to participate in the project. Adequate provisions should be made for
soliciting the independent, non-coerced assent from children or cognitively impaired persons
who are capable of a knowledgeable agreement.

If the person from whom assent is sought refuses, the person should not be enrolled, even
if the parent or legally authorized representative gives permission. The IRB may make an
exception to this guideline in studies of children with life-threatening illnesses who are
eligible for research treatment protocols. Alternatively, if the person from whom assent is sought agrees to participate, the person may not be enrolled if the parent or legally authorized representative does not give permission.

A written informed consent form approved by the IRB and signed (including in an electronic format) is required on all human subjects research that is not exempt from IRB review except as provided in this section. A written copy must be given to the person signing the informed consent form.

The PU-IRB has developed an Informed Consent Document Template that provides investigators with guidance in developing this information. The template is available from the HPA upon request. The template provides prompts to the investigator to add details about the study, levels of risk, and other issues as indicated.

The informed consent requirements in this standard operating procedure are not intended to preempt any applicable Federal, state or local laws (including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that require additional information to be disclosed in order for informed consent to be legally effective.

**Content of the Informed Consent Document**

The informed consent must begin with a concise and focused presentation of the “key information” that is most likely to assist a prospective subject or LAR in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.

It is up to the Parker IRB on a study-by-study basis to determine what information should be included at the beginning of the informed consent in the “key information” section. However, the following information should, at a minimum, be included:

1. The fact that consent is being sought for research and that participation is voluntary.
2. The purposes of the research, the expected duration of the prospective subject’s participation and the procedures to be followed in the research.
3. The reasonably foreseeable risks or discomforts to the prospective subject.
4. The benefits to the prospective subject or to others that may reasonably be expected from the research.
5. Appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the prospective subject.

Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject’s or LAR’s understanding of the
reasons why one might or might not want to participate. No informed consent may include any exculpatory language through which the subject or the LAR is made to waive or appear to waive any of the subject’s legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.

The Informed Consent Document must include all of the following that are applicable to the particular study in question, as described in 45 CFR 46.116 (DHHS) and 21 CFR 50.25 (FDA) or required by the PU-IRB:

1. Title of the project
2. The name of the PI, location of the research, business location of the PI and a study contact person (may be the PI) and their degrees
3. A statement that the study involves research
4. An explanation of the purpose(s) of the research
5. The expected duration of participation
6. A description of the procedures/what will happen during the study and identification of any procedures that are experimental
7. A description of any reasonably foreseeable risks or discomforts to the subject
8. A description of any benefits to subjects or others that may reasonably be expected from the research only
9. Appropriate alternative procedures or courses of treatment, if any
10. Extent to which confidentiality of records identifying subjects will be maintained and a statement that notes those outside the research team who may have access to identified records including regulatory authorities (e.g., DHHS and FDA)
11. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatment is available if injury occurs, and if so, what they consist of and where further information may be obtained
12. Contact information for the principal investigator regarding questions about the research project, and research subjects’ rights, and whom to contact in the event of research-related injury
13. Contact information for the PU-IRB regarding subjects’ rights
14. A statement that participation is voluntary and that refusal to participate or discontinuing participation at any time will involve no penalty or loss of benefits to which the subject is otherwise entitled
15. A statement that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled
16. One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens:
   a. A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized
representative, if this might be a possibility, or
b. A statement that the subject’s information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.

17. The signature and time/date lines for the subject and/or legally authorized representative
18. Signature and time/date lines for person obtaining consent
19. Who is paying for the project, if applicable
20. Footer with page number and space for participant initials
21. Elements of a HIPAA Authorization may be incorporated in the main informed consent document or may be placed in a standalone HIPAA consent document

The federal regulations stipulate that additional elements of informed consent should be provided to the potential subject when appropriate. Based on the study design and in consideration of the subject’s safety and welfare, as well as the relevance of the information in allowing the prospective subject to make an informed decision about participation, PU-IRB may require additional information in the informed consent document including:

1. A statement that the particular treatment or procedure may involve risks to the subject which are currently unforeseeable
2. A statement that the particular treatment or procedure may involve risks to the embryo or fetus, if the subject is or may become pregnant, which are currently unforeseeable
3. Anticipated circumstances under which participation may be terminated by the investigator without regard to the subject’s or the LAR’s consent
4. Any additional costs to the subject that may result from participation in the research
5. Consequences of the subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject
6. A statement that significant new findings developed during the course of a study that may relate to the subject’s willingness to continue will be provided to the subject
7. The approximate number of subjects involved
8. Statement that the subject’s biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit
9. Statement regarding whether clinically relevant research results, including individual research results will be disclosed to subjects, and if so, under what conditions
10. For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (i.e., sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of the specimen)
11. Statement that specifies the patient’s financial responsibilities vs. sponsor responsibilities
12. Clinicaltrials.gov statement
The HPA reviews the informed consent document to determine if all basic elements of consent are contained in the document and if additional elements should be required. The Primary Reviewer also considers the criteria for inclusion of the additional elements of consent. Consent document(s) that are determined to be clearly inappropriate (e.g., significant deficiencies, too complex, reading level greater than 9th grade) are returned to the investigator for re-writing prior to being scheduled for PU-IRB review.

The investigator receives written notice of required changes in the informed consent document prior to final PU-IRB approval. Final approval is not granted until all required changes have been made and submitted for review and approval.

All pages of the approved informed consent document are stamped with the PU-IRB date of approval, and the date of expiration. If the consent document is modified during the protocol approval period, all pages of the informed consent document are stamped with the PU-IRB approval date of the modification, and the date of expiration.

**Posting of Clinical Trial Consent Forms**

For each clinical trial conducted or supported by a Federal department or agency that has adopted the Common Rule (45 CFR 46), one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on the publicly available Federal Web site that was created as a repository for these informed consents. One consent form (any IRB approved version – doesn’t have to be final version) must be posted on the Federal website after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol. A Federal department or agency supporting or conducting the clinical trial may permit or require redactions to the information posted if determined that certain information should not be made publicly available.

**Broad Consent**

The Parker IRB will not be adopting the use of a broad consent. A study specific informed consent or waiver of informed consent, as applicable, may be submitted to the Parker IRB for review.

**Informed Consent Process**

Ethical, professional, federal, and PU-IRB guidelines for human subjects research all require voluntary participation. The roots of this standard are the ethical principles of autonomy and respect from the Belmont Report. The participant must give her or his agreement to participate in the research based upon adequate knowledge and an understanding of relevant information provided under circumstances that minimize the possibilities of coercion or undue influence.
OHRP maintains guidelines that outlines the expectations for the informed consent process for researchers conducting studies at Parker.

**Determining a Potential Adult Subject’s Ability to Consent to Research**

The decision-making capacity of a potential research subject should be evaluated when there are reasons to believe that the subject may not be capable of making voluntary and informed decisions about research participation.

For studies that expect to recruit from populations with disorders known to be associated with impairment of decision-making capacity, the investigator and research staff must have adequate procedures in place for assessing and ensuring subjects’ capacity, understanding, and informed consent or assent. The IRB will evaluate whether the proposed plan to assess capacity to consent is adequate.

For the purpose of this section, a subject has the capacity to consent to his or her own participation in a research activity if s/he demonstrates an appreciation:

1. That the activity is research, not standard treatment
2. Of the risks and benefits of a study
3. Of the alternatives that are available if s/he does not participate
4. That, if s/he chooses not to participate, this decision will be accepted without penalty (i.e., without jeopardizing clinical care)

In reaching a decision about participation, it is essential for the potential subject to demonstrate an ability to use this information in a rational manner. Thus, in considering risks, benefits, and available alternatives, subjects must show they understand the aspects of these factors that are unique to them as individuals. To highlight this distinction, a person who is suffering with severe depression may be able to demonstrate an appreciation of 1, 2, 3 and 4 above, but may not care, or may actually want to take risks. Such individuals should not be considered able to provide consent for themselves.

The assessment of decision-making capacity should be made by a researcher or consultant familiar with dementias and qualified to assess and monitor capacity and consent in such subjects on an ongoing basis. Assessments can be done with at least one of the following methods:

1. A standardized and validated assessment tool
2. A post-consent quiz documenting the subjects’ knowledge of critical elements in the informed consent form
3. Investigator-developed alternative procedures for evaluating the presence of decision-making capacity
Legally Authorized Representative

A legal guardian in the state of Iowa is defined as a person who is not the parent of a child, but who has been appointed by a court or juvenile court having jurisdiction over the child, to have a permanent self-sustaining relationship with the child and to make important decisions which have a permanent effect on the life and development of that child and to promote the general welfare of that child. A guardian may be a court (a district court) or a juvenile court, rather than an individual (Iowa Code 600A.2)

DHHS and the FDA define a legally authorized representative as “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 procedure(s) involved in the research.” (45 CFR 46.102(c); 21 CFR 50.3).

In studies involving children in the state of Texas, the legally authorized representative is:

1. the parent, OR
2. the court-appointed guardian

In studies conducted in the state of Texas involving cognitively impaired adults (adults who may be incompetent or have limited decision-making capacity), the legally authorized representative is:

1. The designated proxy (such as a Durable Power of Attorney for Health Care)
2. Court-appointed guardian
3. Spouse (This does NOT include “common law” spouses)
4. Adult child
5. Parent
6. Adult sibling

In studies involving cognitively impaired adults, permission must be sought from the first existing person reasonably available in the above list, even if another relative is more conveniently available. Not reasonably available means the person is deceased, unknown, incompetent, or unable to provide permission due to inability to communicate with the research team (e.g., the individual is stationed outside the United States in the armed services and does not have access to phone, email, or fax).

15. Permission of Parents/Guardians and Assent by Children

An assent process, either verbal or written, may also be required when the study involves children. The IRB determines and documents when assent is required for all children in the research, for some of the children involved in the research or that assent is not required for any of the children in the research. If the IRB determines that assent is not a requirement for
some of the children in the research, the IRB documents which children are not required to assent.

In making the determination as to whether an assent process will be required, and how assent will be obtained, the PU-IRB considers the age of the subjects, their maturity, and their ability to read and comprehend a written document given their mental and physical capacities and psychological state. If the IRB determines that some or all of the children are limited such that they could not be asked about participation, or if the intervention provided in the research holds out a prospect of direct benefit that is important to the health or well-being of the prospective subject and is available only in the context of the research, the IRB may determine that assent of the child is not required. In addition, even when the IRB determines that some or all children in the proposed research are capable of assenting, the IRB may waive assent when all of the waiver criteria described in the Waiver of Consent or Elements of Consent section below are met. The IRB documents which conditions are applicable when making a determination that assent is not a requirement for some or all of the children in the research.

If the IRB determines that an assent process is required for some or all of the children in the research, the IRB must determine whether or not assent should be documented. If the IRB determines that assent should be documented, the IRB also determines the process to document the assent of the child. Children too young to understand a written consent/assent may be given a verbal explanation in a manner understandable to the child and at a level appropriate for the child’s age, maturity, and condition. When a verbal assent process is used, the investigator must document in some manner that the assent process occurred and that the child provided assent. Any approved assent documents are stamped with PU-IRB date of approval, and the date of expiration.

When children are enrolled in research, the IRB also determines the appropriate provisions for soliciting the permission of each child’s parents or guardians (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). When the IRB determines that the research is no more than minimal risk for the child or is more than minimal risk with the prospect of direct benefit to the child, and the IRB determines that permission must be obtained from the parent(s), the IRB will make a determination whether the permission of one or both parents shall be required.

If the research does not fall into one of these categories, and the IRB determines that permission must be obtained from the parents, then the permission of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available, or if only one parent has legal responsibility for care and custody.

In addition, for children who are wards of the state or any other agency, institution, or entity, they may only be included in research involving greater than minimal risk and no prospect of
direct benefit to individual subjects (45 CFR 46.406) or research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children (45 CFR 46.407) only if:

1. The research relates to their status as a ward, or
2. The research is conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards

If one of the above criteria is met and the research is approved, the IRB requires the appointment of an advocate for each child who is a ward to act on their behalf in addition to their guardian. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child’s participation in the research and who is not otherwise associated in any way (except in the role as advocate or member of the IRB) with the research, researchers, or guardian organization.

The IRB may waive the requirement for parental permission when the criteria described in the Waiver of Consent or Elements of Consent section below are met, or if the IRB determines that parental permission is not a reasonable requirement to protect the child due to the conditions or population under research and the research is not subject to FDA regulations and the waiver is otherwise consistent with Federal, State or local law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe). When this waiver is enacted by the IRB, the IRB determines an appropriate mechanism for protecting the children dependent upon the nature and purpose of the research, the risks, potential benefits, and the children’s age, maturity, status, and condition.

**16. Waiver of Consent or Elements of Consent**

The PU-IRB may approve a consent procedure, which does not include, or which alters, some or all of the elements of informed consent set forth in Section 14: Informed Consent and Documentation of Participation, or it may waive the requirement to obtain informed consent [45 CFR 46.116(3)], provided the PU-IRB finds the research is not FDA-regulated and documents that:

1. The research or demonstration project is to be conducted by, or subject to the approval of, state, local or tribal government officials, and is designed to study, evaluate, or otherwise examine: (i) public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs; and,

2. The research could not practicably be carried out without the waiver or alteration.

PU-IRB may also approve a consent procedure, which does not include, or which alters, some
or all of the elements of informed consent set forth in Section 14: Informed Consent and Documentation of Participation, or it may waive the requirement to obtain informed consent [45 CFR 46.116(3)(f)], provided the PU-IRB finds the research is not FDA-regulated and documents that:

1. The research involves no more than minimal risk to the subjects; and

2. The research could not practicably be carried out without the waiver or alteration; and

3. If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format; and

4. The waiver or alteration will not adversely affect the rights and welfare of the subjects; and

5. Whenever appropriate, the subjects or LAR will be provided with additional pertinent information after participation.

To request a waiver of consent, the investigator must complete the Waiver or Alteration of Consent form and submit it to the IRB via IRBNet.

**Screening, Recruiting or Determining Eligibility**

The Parker IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject’s LAR, if either of the following conditions are met:

1. The investigator will obtain information through oral or written communication with the prospective subject or LAR, or
2. The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens

A waiver of informed consent is not required to conduct the screening or recruiting activities outlined above. The OHRP decision chart (chart 10) below is used to determine if consent can be waived or if consent elements can be altered. It is available at: http://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html
Chart 10: Can Informed Consent Be Waived or Consent Elements Be Altered Under 45 CFR 46.116(c) or (d)?**

**(Note: If subjects include children to whom 45 CFR part 46, subpart D applies, an alternative provision for waiver of parental permission might apply. [See 45 CFR 46.408(c)]

From Chart 8 or 9

Will the research or demonstration project be conducted by or subject to the approval of state or local government officials? [45 CFR 46.116(c)(1)]

Yes →

Is the project designed to study, evaluate, or otherwise examine: (i) Public benefit of service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs? [45 CFR 46.116(c)(1)]

No →

Will the research involve greater than minimal risk, as defined in Section 46.102)? [45 CFR 46.116(d)(1)]

No →

Is it practicable to conduct the research without the waiver or alteration? [45 CFR 46.116(c)(3)]

Yes →

No waiver of informed consent or alteration of consent elements is allowed.*

No →

Will waiving or altering the informed consent adversely affect the subjects’ rights and welfare? [45 CFR 46.116(c)(2)]

Yes →

Will pertinent information be provided to subjects later, if appropriate? [45 CFR 46.116(d)(4)]

Yes →

Waiver of informed consent or alteration of consent elements is allowed if IRB documents these findings and approves waiver or alteration.

No →

If informed consent is not waived entirely

NO →

Go to Chart 11

* Note: See OHRP guidance on informed consent requirements in emergency research at http://www.hhs.gov/ohrp/policy/index.html#emergency for further information on emergency research informed consent waiver.

September 24, 2004
17. Waiver of Documentation of Consent

The PU-IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects. The DHHS regulations [45 CFR 46.117(c)] state that a signed consent form may be waived if the IRB determines one of the following are true:

1. The only record linking the subject and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject or LAR should be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern; or

2. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context; or

3. The subjects or LARs are members of a distinct cultural group or community in which signing forms is not the norm, and the research presents no more than minimal risk of harm to subjects. There must also be an appropriate mechanism for documenting that informed consent was obtained.

The FDA regulations [21 CFR 56.109(c)] state that a signed consent form may be waived if the IRB determines that:

1. The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside the research context; or

2. The requirements in 21 CFR 50.24 for an exception from informed consent for emergency research are met.

In cases in which the documentation requirement is waived, the PU-IRB will determine whether the investigator must provide subjects or LARs with a written statement regarding the research. The PU-IRB reserves the right to request a written statement if it believes providing such will protect the rights or welfare of potential participants.

To request a waiver of documentation of consent, the investigator must complete the Waiver of Documentation of Consent form and submit it to the IRB via IRBNet.

The OHRP decision chart (chart 11) below is used to determine if documentation of Informed Consent can be waived. It is available at:  http://www.hhs.gov/ohrp/regulations-and-policy/decision-charts/index.html
Chart 11: Can Documentation of Informed Consent Be Waived Under 45 CFR 46.117(c)?

From Chart 10

Would the consent document be the only record linking the subject and the research and would the principal risk be potential harm resulting from a breach of confidentiality?
[45 CFR 46.117(c)(1)]

NO

Does the research present no more than minimal risk and involve no procedures for which written consent is normally required outside the research context?
[45 CFR 46.117(c)(2)]

YES

IRB may waive the requirement for a signed consent form for some or all subjects.

AND

IRB may require investigator to provide subjects with a written statement regarding the research.
[45 CFR 46.117(c)]

NO

IF IRB Allows Waiver of Documentation Under 45 CFR 46.117(c)(1)

Investigator will ask each subject if he or she wants documentation linking the subject with the research.
[45 CFR 46.117(c)(1)]

YES

Subject’s wishes will govern whether informed consent is documented.
[45 CFR 46.117(c)(1)]

September 24, 2004
18. Exception from Informed Consent Requirements for Emergency Research

The PU-IRB may consider an exception from informed consent requirements for emergency research for a strictly limited class of research involving activities which may be carried out in human subjects who need emergency therapy and for whom, because of the subjects’ medical condition and the unavailability of legally authorized representatives of the subjects, no legally effective informed consent can be obtained. This exception applies to DHHS and FDA regulated research. However, for DHHS regulated research an exception from informed consent for emergency research cannot be obtained for research involving prisoners (45 CFR 46 Subpart C) or fetuses, pregnant women and human in vitro fertilization (45 CFR 46 subpart B).

The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following:

1. The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions.

2. Obtaining informed consent is not feasible because:
   a. The subjects will not be able to give their informed consent as a result of their medical condition;
   b. The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and
   c. There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation.

3. Participation in the research holds out the prospect of direct benefit to the subjects because:
   a. Subjects are facing a life-threatening situation that necessitates intervention;
   b. Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and
   c. Risks associated with the investigation are reasonable in relation to what is
known about the medical condition of the potential class of subjects, the 
risks and benefits of standard therapy, if any, and what is known about 
the risks and benefits of the proposed intervention or activity.

4. The clinical investigation could not practicably be carried out without the waiver.

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

6. The IRB has reviewed and approved informed consent procedures and an informed 
consent document in accord with Sections 46.116 and 46.117 of 45 CFR 46 for 
DHHS regulated research or 21 CFR 50.25 for FDA regulated research. These 
procedures and the informed consent document are to be used with subjects or 
their legally authorized representatives in situations where use of such 
procedures and documents is feasible. The IRB has reviewed and approved 
procedures and information to be used when providing an opportunity for a family 
member to object to a subject's participation in the clinical investigation consistent 
with the paragraph below.

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

   a. Consultation (including, where appropriate, consultation carried out by the 
      IRB) with representatives of the communities in which the clinical 
      investigation will be conducted and from which the subjects will be drawn;
   b. Public disclosure to the communities in which the clinical investigation will 
      be conducted and from which the subjects will be drawn, prior to initiation 
      of the clinical investigation, of plans for the investigation and its risks and 
      expected benefits;
   c. Public disclosure of sufficient information following completion of the clinical 
      investigation to apprise the community and researchers of the study, 
      including the demographic characteristics of the research population, and 
      its results;
   d. Establishment of an independent data monitoring committee to exercise 
      oversight of the clinical investigation; and
   e. If obtaining informed consent is not feasible and a legally authorized 
      representative is not reasonably available, the investigator has committed, 
      if feasible, to attempting to contact within the therapeutic window the 
      subject's family member who is not a legally authorized representative,
and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review.

The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

The IRB determinations and documentation required by these regulations will be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by the FDA.

Protocols involving an exception to the informed consent requirement, as outlined above, must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists.

If the IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided above or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to the 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. They must also disclose this information to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.
19. Health Insurance Portability and Accountability Act (HIPAA) and Research

Protected health information obtained by a researcher may not be used internally or disclosed to any outside person or organization for research purposes without prior approval of the IRB. Researchers must also abide by all corporate HIPAA policies regarding HIPAA privacy and security.

Waiver or Alteration of the HIPAA Authorization Requirement

For some types of research, it may be impracticable for researchers to obtain written authorization from research participants, for example, for some research conducted on existing databases or repositories where no contact information is available. To address these situations, the Privacy Rule contains criteria for the waiver or alteration of the HIPAA authorization requirement by an IRB [45 CFR 164.512(i)(ii)(2)]. The Privacy Rule permits a covered entity to use or disclose protected health information (PHI) for research purposes without authorization (or with an altered authorization), if the covered entity received proper documentation that an IRB has granted a waiver (or an alteration) of the authorization requirement for the research use or disclosure of PHI.

The PU-IRB serves as a Privacy Board (as defined under the HIPAA regulations) and may approve a consent procedure, which does not include, or which alters, some or all of the elements of the HIPAA consent form, or it may waive the requirement to obtain HIPAA consent if the following criteria are met:

1. The PHI use or disclosure involves no more than a minimal risk to the privacy of individuals based on at least the presence of:
   1) An adequate plan presented to the IRB or Privacy Board to protect PHI identifiers from improper use and disclosure;
   2) An adequate plan to destroy those identifiers at the earliest opportunity, consistent with the research, absent a health or research justification for retaining the identifiers or if retention is otherwise required by law; and
   3) Adequate written assurances that the PHI will not be reused or disclosed to any other person or entity except (a) as required by law, (b) for authorized oversight of the research study, or (c) for other research for which the use or disclosure of the PHI is permitted by the Privacy Rule.

2. The research could not practicably be conducted without the requested waiver or alteration.
3. The research could not practicably be conducted without access to and use of the PHI.

To request a waiver of HIPAA consent, the investigator must complete the Waiver of HIPAA Authorization form and submit it to the IRB.

**Review Preparatory to Research**

The Privacy Rule permits a covered entity to use or disclose protected health information to a researcher without authorization or waiver for the limited purpose of a “review preparatory to research.” Such reviews may be used to prepare a research protocol, or to determine whether a research site has a sufficient population of potential research subjects. Prior to permitting the researcher to access the protected health information, the covered entity must obtain representations from the researcher that the use or disclosure of the protected health information is solely to prepare a research protocol or for similar purposes preparatory to research, that the researcher will not remove any protected health information from the covered entity, and that protected health information for which access is sought is necessary for the research purpose. Researchers should consult the PU-IRB regarding any forms or applications necessary to conduct a review preparatory to research.

Researchers conducting a review preparatory to research may not record information in identifiable form, nor may they use the information that they receive to contact potential subjects, unless the investigator is also the subject’s treating physician. Because the Privacy Rule permits a covered entity to disclose protected health information to the individual who is the subject of the information, covered health care providers and patients may continue to discuss the option of enrolling in a clinical trial without patient authorization. Even when permitted by the Privacy Rule, however, any use of patient information for recruitment must comply with IRB recruitment policies.

Investigators who have previously obtained full consent and authorization to contact a research subject as a result of a previously approved research project, may contact his or her former research subjects provided that the subject agreed to be contacted for information on future research conducted by the same principal investigator or co-investigator(s).

**Research on Protected Health Information of Decedents**

The protections of the Common Rule apply only to living human beings; by contrast, the Privacy Rule also protects the identifiable health information of deceased persons (“decedents”). The Privacy Rule contains an exception to the authorization requirement for research that involves the protected health information of decedents. A covered entity may use or disclose decedents’ protected health information for research if the entity obtains representations from the researcher that the use or disclosure being sought is
solely for research on the protected health information of decedents, that the protected health information being sought is necessary for the research, and, at the request of the covered entity, documentation of the death of the individuals about whom information is being sought. Researchers should submit the applicable IRB forms for IRB approval when they intend to conduct research involving decedents’ protected health information.

**Limited Data Sets with a Data Use Agreement**

When a researcher does not need direct identifiers for a study but does require certain data elements that are not permitted in de-identified data, the Privacy Rule permits a covered entity to disclose a “limited data set” to the researcher without authorization or waiver, provided that the researcher has signed a data use agreement. The limited data set is still considered to be protected health information, but it must exclude only specified direct identifiers of the individual or of relatives, employers, or household members of the individual.

The research involves a limited data set if it removes the following 16 identifiers:

1. Names
2. Postal address info. (if other than city, state and zip)
3. Telephone and fax numbers
4. Email addresses
5. Social Security numbers
6. Medical record, prescription numbers
7. Health plan beneficiary numbers
8. Account numbers
9. Certificate/license numbers
10. Vin and serial numbers, license plate numbers
11. Device identifiers, serial numbers
12. Web URLs
13. IP address numbers
14. Biometric identifiers (finger prints)
15. Full face, comparable photo images

The Privacy Rule requires that the data use agreement used in conjunction with the limited data set contain provisions that:

1. Establish the permitted uses and disclosures of the limited data set by the recipient, consistent with the purposes of the research, and which may not include any use or disclosure that would violate the Rule if done by the covered entity;

2. Limit who can use or receive the data; and

3. Require the recipient to agree to the following:
a. Not to use or disclose the information other than as permitted by the data use agreement or as otherwise required by law;

b. Use appropriate safeguards to prevent the use or disclosure of the information other than as provided for in the data use agreement;

c. Report to the covered entity any use or disclosure of the information not provided for by the data use agreement of which the recipient becomes aware;

d. Ensure that any agents, including a subcontractor, to whom the recipient provides the limited data set agrees to the same restrictions and conditions that apply to the recipient with respect to the limited data set; and

e. Not to identify the information or contact the individual.

Researchers who will be receiving limited data sets must submit a signed copy of the covered entity’s data use agreement to the PU-IRB for approval, prior to initiating the research.

The Privacy Rule contains certain grandfathering provisions that permit a covered entity to use and disclose protected health information for research after the Rule’s compliance date of April 14, 2003, if the researcher obtained any one of the following prior to the compliance date:

1. An authorization or other express legal permission from an individual to use or disclose protected health information for the research;

2. The informed consent of the individual to participate in the research; or

3. An IRB waiver of informed consent for the research.

Even if informed consent or other express legal permission was obtained prior to the compliance date, if new subjects are enrolled or existing subjects are re-consented after the compliance date, the covered entity must obtain the individual’s authorization. For example, if there was a temporary waiver of informed consent for emergency research under the FDA’s human subject protection regulations, and informed consent was later sought after the compliance date, individual authorization must be sought at the same time.

The transition provisions apply to both uses and disclosures of protected health information for specific research protocols and uses or disclosures to databases or repositories maintained for future research.
20. Research with Vulnerable Populations

The PU-IRB requires the investigator to provide sufficient justification for conducting research involving a vulnerable population. The IRB must ensure that all of the regulatory requirements for the protection of vulnerable subjects are met and that appropriate additional protections for vulnerable subjects are in place. Human subjects research should never be conducted using a vulnerable population for the convenience of the research, but only when the vulnerable population at risk in the research activity will also be one of the populations with the potential for benefit from the knowledge gained by the research. Likewise, vulnerable populations should not be excluded from the potential for benefit from research only because there is not a clear statutory rule for obtaining informed consent or the permission of a legally authorized representative.

When the IRB reviews research that involves categories of participants vulnerable to coercion or undue influence, the review process will include one or more individuals who are knowledgeable about or experienced in working with these participants.

45 CFR 46 has additional subparts designed to provide extra protections for vulnerable populations which also have additional requirements for IRBs.

- Subpart B - Additional Protections for Pregnant Women, Human Fetuses and Neonates Involved in Research
- Subpart C - Additional Protections Pertaining to Biomedical and Behavioral Research Involving Prisoners as Subjects
- Subpart D - Additional Protections for Children Involved as Subjects in Research

DHHS and FDA funded research that involves any of these populations must comply with the requirements of the relevant subparts. Research funded by other federal agencies may or may not be covered by the subparts. However, the following policies and procedures, which are based on the subparts, apply to all research regardless of funding at Parker.

Responsibilities

1. The PI is responsible for identifying the potential for enrolling vulnerable subjects in the research proposal. The PI is responsible for identifying subjects who are at risk for impaired decisional capacity, and who are being asked to participate in a research study with greater than minimal risk.

2. The PU-IRB shall include representation, either as members or ad hoc consultants, individual(s) interested in or who have experience with the vulnerable populations involved in the research proposal under review.

3. The PU-IRB reviews the PI’s justifications for including vulnerable populations in the
research to assess appropriateness of the research proposal.

4. The PU-IRB must ensure that additional safeguards have been included in each study to protect the rights and welfare of vulnerable subjects as needed at the time of initial review of the research proposal.

5. The PU-IRB evaluates the proposed plan for consent of the specific vulnerable populations involved. If the research involves adults unable to consent, the IRB evaluates the proposed plan for obtaining permission from legally authorized representatives.

6. The IRB evaluates and approves the proposed plan for the assent of participants.

7. The IRB evaluates the research to determine the need for additional protections and considers the use of a data and safety monitoring board or data monitoring committee, as appropriate.

8. Information reviewed as part of the continuing review process should include the number of participants considered as members of specific vulnerable populations.

9. The IRB should be knowledgeable about and experienced in working with populations who are vulnerable to coercion and undue influence. If the IRB requires additional qualification or expertise to review a protocol, it should obtain consultation.

Children

By regulatory definition, a child is a person who has not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted (45 CFR 46.402(a)). By FDA definition, a child is a person who has not attained the legal age for consent to treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted. For purposes of research conducted in the state of Texas, the term “child” as used in both the DHHS and FDA definitions is analogous to “minor” under Texas Code and is viewed as “a person under 18 years of age who is not and has not been married or who has not had the disabilities of minority removed for general purposes” (Texas Code Sec. 100.003)

In cases of human subjects research under the authority of the PU-IRB but conducted outside of the state of Texas, the PU-IRB may confer with the Parker Legal Counsel regarding the applicability of other local, state, tribal, national, or international laws to the particular project. In general, the PU-IRB will apply the law of the state in which the research is being conducted. For example, if a project involves children and one of the recruitment sites is in a bordering state, the laws of the bordering state will be evaluated to which individuals meet the DHHS and FDA definition of “children” at that site.
Federal regulations permit IRBs to approve a research project involving children after determining which of the following categories applies, and only if the project satisfies all of the conditions in the applicable category [45 CFR 46, Subpart D (DHHS) and 21 CFR 50 Subpart D (FDA)]:

1) Research that does not involve greater than minimal risk may be approved if the IRB finds that adequate provisions are made for soliciting the assent of the children and the permission of their parents or guardians. The IRB may determine that permission of one parent or guardian is sufficient.

2) Research involving greater than minimal risk, but presenting the prospect of direct benefit to an individual subject, or a monitoring procedure that is likely to contribute to the subject's well-being, may be approved if the IRB finds that:
   a. The risk is justified by the anticipated benefit to the subject
   b. The relationship of anticipated benefit to risk is at least as favorable as that presented by available alternative approaches; and
   c. Adequate provisions are made for soliciting the assent of the children and permission of their parents or guardians.

3) Research involving greater than minimal risk with no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition, may be approved if the IRB finds that:
   a. The risk represents a minor increase over minimal risk;
   b. The intervention or procedure presents experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations;
   c. The intervention or procedure is likely to yield generalizable knowledge about the subject's disorder or condition which is of vital importance for the understanding or amelioration of the subject's disorder or condition; and
   d. Adequate provisions are made for soliciting assent of the children and permission of their parents or guardians.

4) Research that is not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children may be approved if the IRB and the Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines and following an opportunity for public review and comment, find that:
a. The research in fact satisfies one of the above three conditions; or

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

c. The research will be conducted in accordance with sound ethical principles; and adequate provisions are made for soliciting the assent of children and the permission of their parents or guardians.

In compliance with federal regulations, the IRB must determine that permission of both parents is required, unless one parent is deceased, unknown, incompetent, or not reasonably available, or unless only one parent has legal responsibility for the care and custody of the child.

Federal regulations [45 CFR 46.409(b)] also indicate that children who are wards of the state, or any other agency, institution, or entity can only be included in research in this category if the research is related to their status as wards or conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards. If one of these criteria is met and the research is approved, the IRB must require appointment of an advocate for each child who is a ward in addition to the person acting as guardian or in loco parentis. One person may serve as the advocate for multiple wards, however this advocate must have the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child’s participation in the research and cannot be associated in any way (except as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

**Pregnant Women, Human Fetuses and Neonates**

Federal regulations direct that IRBs require additional safeguards before approving research involving fetuses, pregnant women, or neonates (45 CFR 46, Subpart B).

The IRB may approve research involving pregnant women or fetuses if all of the following conditions are met:

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

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

4. If the research holds out the prospect of direct benefit to the pregnant woman, the 
   prospect of direct benefit both to the pregnant woman and the fetus, or no 
   prospect of benefit for the woman nor the fetus when risk to the fetus is not greater 
   than minimal and the purpose of the research is the development of important 
   biomedical knowledge that cannot be obtained by any other means, the woman’s 
   consent is obtained OR

5. If the research holds out the prospect of direct benefit solely to the fetus, then the 
   consent of the pregnant woman and the father is obtained except that the father’s 
   consent need not be obtained if he is unable to consent because of unavailability, 
   incompetence, or temporary incapacity or the pregnancy resulted from rape or 
   incest;

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

7. For children who are pregnant, assent and permission are obtained in accord with 
   the regulations for children in research (45 CFR 46, Subpart D);

8. No inducements, monetary or otherwise, will be offered to terminate a pregnancy;

9. Individuals engaged in the research will have no part in any decisions as to the 
   timing, method, or procedures used to terminate a pregnancy; and

10. Individuals engaged in the research will have no part in determining the viability of 
    the neonate.

When a child is screened in a study or participating in study procedures that require a 
    pregnancy test be administered, additional consent and assent information must be 
    provided in the Informed Consent Document. The IRB has determined that children in 
    research must be afforded the same rights they would normally have in a clinical setting 
    with regard to the privacy of results from pregnancy testing. Thus, minors 12 years of age 
    would have the choice as to whether or not pregnancy results would be shared with their 
    parents/legal guardians. For children who have a positive pregnancy test and are less than 
    12 years of age, or if abuse is expected at any age, the proper authorities must be informed 
    and parents or guardians will be informed of the pregnancy.

Neonates, 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 is fully informed regarding the reasonably foreseeable impact of the research on the neonate;

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

4. The requirements regarding neonates of uncertain viability (see below) or nonviable neonates (see below) have been met as applicable.

**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

2. 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

3. The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent’s legally authorized representative is obtained in accord with 45 CFR 46 Subpart A (except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest).

**Nonviable Neonates**

After delivery, 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 45 CFR 46 Subpart A (note: waiver or alteration of the consent does not
apply here) 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 except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of the legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements.

**Viable Neonates**

A neonate, after delivery, that has been determined to be viable may be included in the research only to the extent permitted by and in accord with the requirements for children involved in research (45 CFR Subparts A and D)

Research not otherwise approvable will only be allowed in this vulnerable population if:

1. The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates; AND

2. The Secretary of DHHS, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following an opportunity for public review and comment, including a public meeting announced in the Federal Register has determined that the research may take place.

3. Research involving human fetal tissue (placenta, or tissue from a spontaneous or induced abortion or from a stillbirth) is evaluated as tissue specimen research, using the guidelines for research involving specimens.

**Prisoners**

Because incarceration could affect a person's ability to make a truly voluntary and uncoerced decision whether or not to participate in a research project, the federal regulations provide additional safeguards for the protection of prisoners (45 CFR 46, Subpart C). A prisoner is defined as any individual involuntarily confined or detained in a penal institution. This definition includes individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

At Parker, any project that recruits prisoners must be reviewed at a full IRB meeting with a prisoner advocate present. If the project was not initially approved to recruit prisoners, then the investigator may not enroll a prisoner (e.g., a prisoner who is brought to Parker for treatment who happens to be eligible for a research study may not be enrolled unless
the PU-IRB application indicates the enrollment of prisoners.)

Federal regulations pertaining to prisoners also apply for a subject who at a later date becomes a prisoner, because it is unlikely that the IRB review of the research project contemplated the constraints imposed by incarceration. Therefore, if an investigator determines that a subject has become a prisoner at some later date after enrollment, and the study involves additional research interventions or interactions with that subject, the subject must either be dropped from follow-up, or a modification application must be submitted requesting review for inclusion of prisoners as subjects.

When a prisoner is a subject, in addition to the usual criteria for approval, the IRB must find that:

1. The research under review represents one of the categories of research permissible under 45 CFR 46.306(a)(2);
   a. Study of the possible causes, effects, and processes of incarceration, and of criminal behavior, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
   b. Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subjects;
   c. Research on conditions particularly affecting prisoners as a class (for example, research on social and psychological problems such as alcoholism, drug addiction, and sexual assaults);
   d. Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health or well-being of the subject.

2. Any possible advantages accruing to the prisoner through his or her participation in the research, when compared to the general living conditions, medical care, quality of food, amenities and opportunity for earnings in the prison, are not of such a magnitude that his or her ability to weigh the risks of the research against the value of such advantages in the limited choice environment of the prison is impaired;

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

4. Procedures for the selection of subjects within the prison are fair to all prisoners and immune from arbitrary intervention by prison authorities or prisoners. Unless the principal investigator provides to the Board justification in writing for following some other procedures, control subjects must be selected randomly from the group
of available prisoners who meet the characteristics needed for that particular research project;

5. The information is presented in language which is understandable to the subject population;

6. Adequate assurance exists that parole boards will not consider a prisoner's participation in the research in making decisions regarding parole, and each prisoner is clearly informed in advance that participation in the research will have no effect on his or her parole; and

7. Where the Board 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, considering the varying lengths of individual prisoners' sentences, and for informing participants of this fact.

The informed consent document must include additional information for potential subjects regarding the fact that participation or non-participation will have no effect on the duration of incarceration or terms of parole. For the review of research involving prisoners, a majority of the IRB members (exclusive of prisoner members) shall have no association with the prison involved, apart from their membership on the IRB. At least one member of the Board shall be a prisoner, or a prisoner representative with appropriate background and experience to serve in that capacity, except that where a particular research project is reviewed by more than one Board only one Board need satisfy this requirement.

**Expedited Review of Research Including Prisoners**

Research involving interaction with prisoners may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied. The prisoner advocate must concur with the determination that the research involves no greater than minimal risk. The prisoner advocate must review the research as a reviewer, designated by the chair, or consultant. Review of modifications and continuing review must use the same procedures for initial review using this expedited procedure including the responsibility of the prisoner advocate.

Research that does not involve interaction with prisoners (e.g. existing data, records review) may be reviewed by the expedited procedure, if a determination is made that the research involves no greater than minimal risk for the prison population being studied. Review by a prisoner advocate is not required. The prisoner advocate may review the research as a reviewer or consultant if designated by the IRB chair. Review of modifications and continuing review must use the same procedures as initial review.
Certification to DHHS for Research Including Prisoners

Under 45 CFR 46.305(c), the institution responsible for conducting research involving prisoners that is supported by HHS shall certify to the Secretary (through OHRP) that the IRB has made the seven findings required under 45 CFR 46.305(a). For all HHS conducted or supported research the PU-IRB will send to OHRP a certification letter to this effect, which will also include the name and address of the institution and specifically identify the research protocol in question and any relevant HHS grant application or protocol. HHS conducted or supported research involving prisoners as subjects may not proceed until OHRP issues its approval in writing on behalf of the Secretary under 45 CFR 46.306(a)(2).

Under its authority at 45 CFR 46.115(b), OHRP requires that the institution responsible for the conduct of the proposed research also submit to OHRP a copy of the research proposal so that OHRP can determine whether the proposed research involves one of the categories of research permissible under 45 CFR 46.306(a)(2), and if so, which one. The term "research proposal" includes the IRB-approved protocol, any relevant HHS grant application or proposal, any IRB application forms required by the IRB, and any other information requested or required by the IRB to be considered during initial IRB review. The above requirement does not apply to research that is not HHS conducted or supported.

Subjects who Lack Decision-Making Capacity

The requirements in this section apply to all research involving persons with mental disabilities or persons with impaired decision-making capacity regardless of funding source.

Research involving persons with impaired decision-making capability may only be approved when the following conditions apply:

1. Only incompetent persons or persons with impaired decision-making capacity are suitable as research subjects. Competent persons are not suitable for the proposed research. The investigator must demonstrate to the PU-IRB that there is a compelling reason to include incompetent individuals or persons with impaired decision-making capacity as subjects. Incompetent persons or persons with impaired decision-making capacity must not be subjects in research simply because they are readily available.

2. The proposed research entails no significant risks, tangible or intangible, or if the research presents some probability of harm, there must be at least a greater probability of direct benefit to the participant. Incompetent people or persons with impaired decision-making capacity are not to be subjects of research that imposes a risk of injury, unless that research is intended to benefit that subject and the probability of benefit is greater than the probability of harm.
3. Procedures have been devised to ensure that participant’s representatives are well informed regarding their roles and obligations to protect incompetent subjects or persons with impaired decision-making capacity. The surrogate should make decisions based upon the subject’s known preferences. If the subject’s preference is unknown, decisions should be based on a judgment of what the subject’s preference would be in the given situation or based on what is in the subject’s best interest, in general.

For research protocols involving subjects who have fluctuating or limited decision-making capacity the IRB may ensure that investigators establish and maintain ongoing communication with involved caregivers. Periodic re-consent should be considered in some cases. Third party consent monitors may be used during the recruitment and consenting process, or waiting periods may be required to allow more time for the subject to consider the information that has been presented.

In the event research participants become incompetent or impaired in decision making capacity after enrollment, the PI is responsible for notifying the IRB and HPA. The PI is responsible for developing a monitoring plan which follows the guidelines outlines above for incompetent and impaired decision-making research participants.

The criteria outlined in the Determining a Potential Adult Subject’s Ability to Consent to Research section should be used to determine decision-making capacity.

Subjects Whose Primary Language is not English

The requirements in this section apply to research involving non-English speaking subjects (1) for research targeting a specific subject population that is non-English speaking or that reasonably anticipates that a proportion of the subjects may be non-English speaking and (2) if a non-English speaking subject is unexpectedly encountered.

The federal regulations [45 CFR 46.116 and 21 CFR 50.20] require that informed consent information be presented to a research subject in a language that is understandable to that subject.

In order to comply with federal regulations, if a subject cannot speak English, then special procedures for the consent process must be followed. There are two acceptable methods for enrolling subjects in research when they are non-English speaking.

1. If the research targets a specific subject population that is non-English speaking or it is reasonably anticipated that, based upon the recruitment procedures, a proportion of the subjects may be non-English speaking, then the entire consent document, including recruitment materials, must be translated into the other language(s). The translated
document must be approved by the IRB before it is used in the research. The IRB recommends obtaining approval for the English version of the consent document first, then submitting other language translations of the consent as an amendment. The person translating the consent document should be qualified or certified in translation and a description of the qualifications of the person conducting the translation should be submitted with the amendment. The translator (or better yet a different person) should back translate the document, checking for accuracy. If the investigator is not fluent in the language used to present the consent document, a translator may be used during the consent process. Study records should document the use of a translator. There must be a witness to the translation process and the researcher should include a statement in the research records (and on the English language consent form) to indicate that the translation took place, identify the translator, and document the translator's belief that the subject understands the research and the consent process. If the subject is a patient, a note about the translation should be made in the subject's research and medical record as well.

2. An investigator cannot always anticipate needing a consent document in another language. In this instance, the regulations do allow the use of a ‘short form’ consent document [45 CFR 46.117 (b) (2), 21 CFR 50.27 (b) (2)]. The short form is a document written in language understandable to the subject that outlines the information the subject will be told about the research. When using a ‘short form’ to document consent, the informed consent must begin with a concise and focused presentation of the key information to assist a prospective subject in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension. The investigator would then have an information sheet read to the subject in their language, usually by a translator. The information sheet may be the IRB approved English version of the consent document or another summary of the research that has been IRB approved. If the information sheet is not the English consent document, then a separate summary document must be IRB approved. Once the information sheet is orally presented to the subject in their language, the short form should be signed by the subject (or the Legally Authorized Representative [LAR]) and then a witness. The summary document should be signed by the person obtaining consent and the witness. The person witnessing the consent process must be fluent in English and the other language and must witness the entire consent process. The translator may serve as the witness. Copies of both the short form and the summary must be given to the subject. The English version and all language versions of the short form that will be used by an investigator must be IRB approved and may be approved via the expedited review procedures as an amendment.

NOTE: The translator may not be a friend or member of the potential subject’s family.

It is important to think about the logistics of enrolling a subject that does not fully understand English. The FDA information sheets caution, “Investigators should carefully consider the ethical/legal ramifications of enrolling subjects when a language barrier exists. If the subject does not clearly understand the information presented, the subject's consent will not truly be
informed and may not be legally effective.” Remember that consent is a process and in order for the subject to enroll and continue in the research, the investigator and his/her staff must be able to communicate adequately with the subject throughout the research or it is possible that the subject may be put at risk. It is possible that the subject’s compliance or data integrity may be jeopardized by the subject’s lack of understanding of the research.

**Illiterate English-Speaking Subjects**

If a person who speaks and understands English, but does not read and write is unexpectedly encountered, they can be enrolled in a study by "making their mark" on the consent document, when consistent with applicable state law.

A person who can understand and comprehend spoken English can be entered into a study if they are competent and able to indicate approval or disapproval by other means. The IRB may approve an oral consent process, provided the subject (1) retains the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally (still competent) and (2) is able to indicate approval or disapproval to study entry.

For research that is no more than minimal risk, documentation of consent may be waived according to the criteria in Section 17: Waiver of Documentation of Consent.

For more than minimal risk research, the consent form must be read to the subjects and the subjects must be given an opportunity to ask questions. An audiotape approved by the IRB may be used. If capable of doing so, the subject signs, or marks an X to signify consent. If that is not possible, the subject will provide verbal consent. The person obtaining consent and a witness will sign the written study consent form with a statement that documents that an oral process was used and, if necessary, that the subject gave verbal consent. The consent process will also be documented in the medical record and research record. Signed copies of the consent form are given to the subject and, whenever possible, these documents should be provided to the subject on audio or video tape.

**Subjects Physically Unable to Talk or Write**

An individual who can understand and comprehend spoken English, but is physically unable to talk or write, may be entered into a study if they:

1. Retain the ability to understand the concepts of the study and evaluate the risk and benefit of being in the study when it is explained verbally (i.e., are competent), and
2. Are able to indicate approval or disapproval to study entry.

The consent form should document the method used for communication with the prospective subject and the specific means by which the prospective subject communicated agreement to
participate in the study. An impartial third party should witness the entire consent process and sign the consent document. A video tape recording of the consent interview is recommended.

**Subjects Unable to Hear**

For deaf subjects who are fluent in American Sign Language (ASL), the IRB may approve a consent process using ASL and the IRB-approved written consent form. When this process is approved, the individual authorized to consent prospective subjects must use an interpreter fluent in ASL to conduct the consent process. There must be a witness to the translation process and the researcher should include a statement in the research records (and on the consent form) to indicate that the translation took place, identify the translator, and document the translator’s belief that the subject understands the research and the consent process. If the subject is a patient, a note about the translation should be made in the subject's research and medical record as well.

**NOTE: The translator may not be a friend or member of the potential subject’s family.**

**21. Research Using FDA Regulated Products**

FDA regulations apply to any research that involves a test article in a clinical investigation involving human subjects as defined by the FDA regulations. For FDA regulated research, the IRB must apply the FDA regulations at 21 CFR 50 and 21 CFR 56, as well as, where appropriate, 45 CFR 46.

Parker University does not conduct drug research. Use of an investigational device in a clinical trial to obtain safety and effectiveness data must be conducted according to FDA’s IDE regulations, 21 CFR Part 812, and other applicable FDA regulations.

The following procedures describe the review of FDA-regulated research conducted by the PU-IRB.

**IDE Requirements**

Researchers who employ a test article classified by the Food and Drug Administration as an investigational device (IDE) must assure the IRB that they are complying with the FDA's regulations (including 21 CFR 50, 56, 312, 320 600, and 812). If applicable, the IDE letter from the FDA including the number assigned to the test article/device must be filed with the IRB when the application for review is submitted.

The HPA will confirm that the IDE number provided in the IRB submission matches that recorded on the sponsor protocol, communication from the sponsor, or communication from the FDA. Validation of the IDE number is required before IRB approval can be granted.
If the research involves drugs or devices and there is no IDE, the PI must provide a rationale why it is not required.

The IRB will review the application and determine:

1. Whether there is an IDE and if so, whether there is appropriate supporting documentation

2. If the research involves devices with no IDE, and whether the research meets the criteria for IDE exemption

**Investigational Devices**

An investigational device is a medical device that is the subject of a clinical investigation. Clinical investigations conducted to evaluate safety and effectiveness of medical devices must be conducted according to the requirements of the IDE regulations [21 CFR part 812]. Certain clinical studies of devices (e.g., certain studies of lawfully marketed devices) may be exempt from the IDE regulations [21 CFR 812.2(c)].

Unless exempt from the IDE regulations, an investigational device must be categorized as either "significant risk" (SR) or "nonsignificant risk" (NSR). A significant risk (SR) device is one that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. A nonsignificant risk (NSR) device is one that does not meet the definition for SR.

The risk determination is based on the proposed use of a device in an investigation, and not on the device alone. In deciding if a study poses a SR, the PU-IRB considers the nature of the harm that may result from use of the device. Studies where the potential harm to subjects could be life-threatening, could result in permanent impairment of a body function or permanent damage to body structure, or could necessitate medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to body structure are considered SR. Also, if the subject must undergo a procedure as part of the investigational study (e.g., a surgical procedure), the PU-IRB considers the potential harm that could be caused by the procedure in addition to the potential harm caused by the device.

The determination that a device presents a nonsignificant or significant risk is initially made by the sponsor. The proposed study is then submitted either to FDA (for SR studies) or to an IRB (for NSR studies). The FDA and/or the IRB will confirm the categorization of the device.

To help in the determination of the risk status of the device, an investigator is asked to
include the sponsor’s (including the investigator on investigator-initiated studies) assessment of whether or not a device study presents a significant or nonsignificant risk. The investigator must provide the PU-IRB with a description of the device, reports of prior investigations with the device, the proposed investigational plan, a description of subject selection criteria, and monitoring procedures. The investigator must inform the PU-IRB whether other IRBs have reviewed the proposed study and what determination was made. The investigator must inform the PU-IRB of the FDA’s assessment of the device's risk if such an assessment has been made. The PU-IRB may also consult with FDA for its opinion.

The PU-IRB may agree or disagree with the investigator/sponsor's initial NSR assessment. If the PU-IRB agrees with the sponsor's initial NSR assessment and approves the study, the study may begin without submission of an IDE application to the FDA. If the PU-IRB disagrees, the sponsor should notify the FDA that an SR determination has been made and the initiation of the study must be delayed until FDA approval of an IDE application has been granted.

If the PU-IRB decides the device/study is significant risk, it notifies the investigator of this decision. The PU-IRB must be provided with notice that an IDE has been granted, and the IDE number must appear on the investigator’s PU-IRB application prior to final full Board review.

Once the SR/NSR decision has been reached and proper documentation provided, the PU-IRB considers whether the study should be approved or not. Full PU-IRB review is required for the initial review of all studies involving investigational devices. Studies that are determined to include NSR devices and that include no other risks that are considered more than minimal risk may be determined by the Board to meet the criteria for expedited continuing review. The criteria for deciding if SR and NSR studies are approved are the same as for any other study. Minutes of the PU-IRB meetings document the rationale for SR/NSR and subsequent approval or disapproval decisions for the clinical investigation.

The IRB's SR/NSR determination has significant consequences for the study sponsor, FDA, and prospective research subjects. SR device studies must be conducted in accordance with the full IDE requirements [21 CFR part 812], and may not commence until FDA and IRB approval are granted. Submission of the IDE application enables the FDA to review information about the technical characteristics of the device, the results of any prior studies (laboratory, animal and human) involving the device, and the proposed study protocol and consent documents. Based upon the review of this information, the FDA may impose restrictions on the study to ensure that risks to subjects are minimized and do not outweigh the anticipated benefits to the subjects and the importance of the knowledge to be gained.

In contrast, NSR device studies do not require submission of an IDE application to the FDA. Instead, the sponsor is required to conduct the study in accordance with the "abbreviated requirements" of the IDE regulations [21 CFR 812.2(b)]. Unless otherwise notified by the
FDA, an NSR study is considered to have an approved IDE if the sponsor fulfills the abbreviated requirements. The abbreviated requirements address, among other things, the requirements for IRB approval and informed consent, recordkeeping, labeling, promotion, and study monitoring. If a sponsor has identified a study as NSR, then the investigator must provide an explanation of the determination. If the FDA has determined that the study is NSR, documentation of that determination must be provided. NSR studies may commence immediately following IRB approval.

Additional information on medical device studies is available at:


**IDE Exemptions**

For devices, an IDE is not necessary if:

1. The research involves a device, other than a transitional device, in commercial distribution immediately before May 28, 1976, when used or investigated in accordance with the indications in labeling in effect at that time;

2. The research involves a device other than a transitional device, introduced into commercial distribution on or after May 28, 1976, that the FDA has determined to be substantially equivalent to a device in commercial distribution immediately before May 28, 1976, and that is used or investigated in accordance with the indications in the labeling FDA reviewed under subpart E of 21 CFR 807 in determining substantial equivalence;

3. The research involves a diagnostic device, if the sponsor complies with applicable requirements in 21 CFR 809.10(c) and if the testing:
   a. Is noninvasive,
   b. Does not require an invasive sampling procedure that presents significant risk,
   c. Does not by design or intention introduce energy into a subject, and
   d. Is not used as a diagnostic procedure without confirmation of the diagnosis by another, medically established diagnostic product or procedure;

4. The research involves a device undergoing consumer preference testing, testing of a modification, or testing of a combination of two or more devices in commercial distribution, if the testing is not for the purpose of determining safety or effectiveness and does not put subjects at risk;

5. The research involves a device intended solely for veterinary use;
6. The research involves a device shipped solely for research on/or with laboratory animals and labeled in accordance with 21 CFR 812.5(c); or

7. The research involves a custom device as defined in 21 CFR 812.3(b), unless the device is being used to determine safety or effectiveness for commercial distribution.

**Emergency Use of an Investigational Device**

The FDA human subjects regulations allow for an investigational device to be used in emergency situations without prior IRB approval. Emergency use is defined as a life-threatening situation in which no standard acceptable treatment is available and in which there is not sufficient time to obtain IRB approval for the use [21 CFR 56.102(d)]. The emergency use provision in the FDA regulations [21 CFR 56.104(c)] is an exemption from prior review and approval by the IRB. The investigator is still required to obtain informed consent under these circumstances unless the FDA requirements in 21 CFR 50.23(a)-(c) allowing an exception to the requirement for informed consent are met.

Whenever possible the PU-IRB requires the investigator to notify the IRB and receive acknowledgement of the emergency use from the IRB Chair (or IRB member designee) before administering the test article. The IRB Chair (or IRB member designee) reviews the application for emergency use and acknowledges whether or not they concur that administering the test article in this situation meets the emergency use requirements at 21 CFR 56.102(d). The acknowledgement by the IRB does not represent approval as FDA regulations do not allow expedited approval of research in emergency situations. It should be noted that manufacturers’ policies typically require an acknowledgement or approval letter from the IRB before the test article will be shipped.

The emergency use exemption for an investigational drug, biologic or medical device requires that each of the following criteria in 21 CFR 56.102(d) is satisfied:

1. A “life-threatening” situation exists;
2. No standard acceptable treatment is available; and
3. Insufficient time is available to obtain IRB approval at a convened meeting.

The term “life-threatening” encompasses conditions that are either:

1. Life-threatening: diseases or conditions where the likelihood of death is high unless the course of the disease is interrupted and diseases or conditions with potentially fatal outcomes, where the end point of clinical trial analysis is survival. The criteria for life-threatening do not require the condition to be immediately life-threatening or to immediately result in death. Rather, the subject must be in a life-threatening situation requiring intervention before review at a convened meeting of the IRB is feasible.
2. Severely debilitating: diseases or conditions that cause major irreversible morbidity. Examples of severely debilitating conditions include blindness; loss of arm, leg, hand or foot; loss of hearing; paralysis or stroke.

The emergency use of a test article must be reported to the IRB within five working days [21 CFR 56.104(c)]. The written report submitted to the PU-IRB Chair after emergency use must include a cover letter explaining the medical condition, reason for use, date administered and independent assessment of use by an uninvolved physician as well as a copy of the signed informed consent document and protocol, if available. The investigator must also include any manufacturer information available on the product (e.g., device brochure). All emergency use reports are reviewed at a convened meeting of the IRB.

The investigator’s report is presented at the next PU-IRB meeting. When the PU-IRB receives a report by an investigator of an emergency use, the PU-IRB examines the case to assure that the emergency use was justified. If the PU-IRB determines that the emergency use was not justified, this is considered noncompliance and the noncompliance procedures are followed. Since prior IRB approval is not obtained, the patient may not be considered a research subject under DHHS regulations 45 CFR 46, but is considered a human subject under FDA regulations 21 CFR 56.102.

Although this procedure is designed to permit only a single emergency use of a test article for the treatment of one patient by one physician within Parker, it is not intended to limit the authority of a physician to provide emergency care in a life-threatening situation. Should a situation arise which would require the emergency use of the test article for a second patient, either by the same or a second physician, for the same test article, subsequent emergency use should not be withheld for the purpose of gaining IRB approval. If it appears probable that similar emergencies will require subsequent use of the test article at Parker, every effort should be made either to sign on to the sponsor's protocol or to develop a protocol for future use of the article at the institution. Either of these protocols would need to be prospectively reviewed and approved by the PU-IRB for future use of the test article. The use of a test article in an investigation designed to be conducted under emergency conditions (e.g., emergency room research) usually does not qualify for the emergency use exemption.

Expanded Access to Investigational Devices

Sometimes, investigational products are used for treatment of serious or life-threatening conditions either for a single subject or for a group of subjects, because there are not comparable or satisfactory alternative treatment options. An investigator planning to use any of the expanded access avenues should contact the PU-IRB before submitting an application to the IRB. All protocols for expanded access must be reviewed and approved by the PU-IRB prior to implementation. The PU-IRB follows FDA regulations and guidance related to the
following types of expanded access to investigational devices:

- Compassionate Use (Single Patient/Small Group Access) – 21 CFR 812.35(a)
- Treatment IDE – 21 CFR 812.36
- Continued Access

22. Investigator Responsibilities

In order to satisfy the requirements of this policy, investigators who conduct research involving human subjects must:

1. Develop and conduct research that is in accordance with the ethical principles in the Belmont Report

2. Develop a research plan that is scientifically sound and minimizes risk to the subjects;

3. Have sufficient resources necessary to protect human subjects, including:
   a. Access to a population that would allow recruitment of the required number of subjects.
   b. Sufficient time to conduct and complete the research.
   c. Adequate numbers of qualified staff.
   d. Adequate facilities.
   e. A process to ensure that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions.
   f. Availability of medical or psychological resources that subjects might require as a consequence of the research.

4. Assure that all procedures in a study are performed with the appropriate level of supervision and only by individuals who are licensed or otherwise qualified to perform such under the laws of Iowa and the policies of the PU-IRB;

5. Assure that all authorized study personnel are educated in the regulatory requirements regarding the conduct of research and the ethical principles upon which they are based;

6. Protect the rights and welfare of prospective subjects;

7. Ensure that risks to subjects are minimized: (i) By using procedures which are consistent with sound research design and which do not unnecessarily expose subjects to risk, and (ii) whenever appropriate, by using procedures already being performed on the subjects for diagnostic or treatment purposes

8. Recruit subjects in a fair and equitable manner
9. Obtain and document informed consent as required by the IRB and ensure that no human subject is involved in the research prior to obtaining their consent;

10. Have plans to monitor the data collected for the safety of research subjects;

11. Protect the privacy of subjects and maintain the confidentiality of data;

12. When some or all of the subjects are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, include additional safeguards in the study to protect the rights and welfare of these subjects;

13. Have a procedure to receive complaints or requests for additional information from subjects and respond appropriately;

14. Ensure that pertinent laws, regulations, and institutional procedures and guidelines are observed by participating investigators and research staff;

15. Ensure that all research involving human subjects receives IRB review and approval in writing before commencement of the research;

16. Comply with all IRB decisions, conditions, and requirements;

17. Ensure that protocols receive timely continuing IRB review and approval;

18. Report unanticipated problems involving risk to subjects or others and any other reportable events to the IRB;

19. Obtain IRB review and approval in writing before changes are made to approved protocols or consent forms; and

20. Seek IRB assistance when in doubt about whether proposed research requires IRB review

23. **Required Trainings**

All individuals engaged in research using human subjects at Parker are required to be familiar with the PU-IRB Standard Operating Procedures and related federal regulations. They are also required to complete human subjects protection training, conflicts of interest in research training and conflicts of interest disclosure prior to submitting a research study to the PU-IRB for review.
Protecting Human Research Participants

All investigators conducting human subjects research at Parker Health System are required to complete the Protecting Human Research Participants training, or equivalent, one-time to become "certified" in human subject protections. This educational requirement applies to all members of the research team, including the principal investigator and all other individuals who have contact or interactions with research subjects or with their private, identifiable information.

Conflicts of Interest in Research

Federal regulations place the responsibility for determining the existence of a financial conflict of interest in research on the institution. Researchers must disclose all financial interests in outside entities, annually. The PU-IRB reviews the disclosures annually or when a change in COI is reported. The Conflicts of Interest – Research policy applies to all individuals involved in research at Parker Health System who contribute in a substantive way to the development, execution, and reporting of research, and who are granted a significant degree of freedom in exercising independent judgment.

Researchers that are participating in studies that are funded by the Public Health Service also must complete a Conflicts of Interest in Research training course once every four (4) years. This training can be found in HealthStream.

Conflicts of interest in research involve situations in which an investigator has a significant financial or associational interest that may compromise, or have the appearance of compromising, professional judgment in the design, conduct, or reporting of research.

24. Record Retention Policy

The HPA maintains copies of the following items following completion or termination of the research study:

1. Copies of all research proposals reviewed, scientific evaluations, if any, that accompany the proposals, approved sample consent documents, progress reports submitted by investigators, and reports of injuries to subjects.

2. Minutes of IRB meetings which shall be in sufficient detail to show attendance at the meetings; actions taken by the IRB; the vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.
3. Records of continuing review activities.

4. Copies of all correspondence between the IRB and the investigators.

5. A list of IRB members in the same detail as described in 45 CFR 46.103(b)(3).

6. Written procedures for the IRB in the same detail as described in 45 CFR 46.103(b)(4) and 45 CFR 46.103(b)(5).

7. Statements of significant new findings provided to subjects, as required by 45 CFR 46.116(b)(5).

All records are retained for a minimum of 3 years for studies that do not involve protected health information, or six years for studies that involve protected health information. The records are accessible for inspection and copying by authorized representatives of federal agencies or departments at reasonable times and in a reasonable manner in accordance with 21 CFR 56.115(b) and 45 CFR 46.115(b).

Retained records dating prior to November 2008 are kept by the PU-IRB in paper format within the HPA office. All records after 2008 are available within IRBNet.

25. Definitions

**Adverse Event** - any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research (modified from the definition of adverse events in the 1996 International Conference on Harmonization E-6 Guidelines for Good Clinical Practice).

**Assent** - agreement by an individual not competent to give legally valid informed consent (e.g., a child or cognitively impaired person) to participate in research.

**Associational Interest** - an interest that stems from an individual’s or entity’s formal or informal participation in or involvement with (directly or indirectly such as through a family member) an organization or entity that, in turn, has a financial or economic stake in an industry entity engaged in research activities.

**Belmont Report** - a statement of basic ethical principles governing research involving human subjects issued by the National Commission for the Protection of Human Subjects in 1978.

**Benign Behavioral Intervention** – interventions that are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing.
Children (Child) –

DHHS definition: persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted.

FDA definition: persons who have not attained the legal age for consent to treatments or procedures involved in clinical investigations, under the applicable law of the jurisdiction in which the clinical investigation will be conducted.

**For purposes of research conducted in Iowa, the term “child” as used in both the DHHS and FDA regulations is analogous to “minor” under Iowa Code and is viewed as “an unmarried person under the age of eighteen years.” [Based on Iowa Code §600A.2 (13)]

Clinical Investigation –

FDA definitions: any experiment that involves a test article and one or more human subjects and that is one of the following:

1. subject to requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or
2. is not subject to requirements for prior submission to the Food and Drug Administration under these sections of the act but the results of which are intended to be submitted later to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.
3. The term does not include experiments that are subject to the provision of 21 CFR 58, regarding nonclinical laboratory studies. [From 21 CFR 50.3(c); 21 CFR 56.102(c)]

The terms research, clinical research, clinical study, study, and clinical investigation are deemed to be synonymous for purposes of this part. [21 CFR 56.102(c)]

For an activity involving drugs: “Clinical investigation means any experiment in which a drug is administered or dispensed to, or used involving, one or more human subjects. For the purposes of this part, an experiment is any use of a drug except for the use of a marketed drug in the course of medical practice.” [21 CFR 312.3(b)]

For an activity involving devices: “Investigation means a clinical investigation or research involving one or more subjects to determine the safety or effectiveness of a device.” [21 CFR 812.3(h)]

“Test article means any drug (including a biological product for human use), medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the act or under sections 351 and 354-360F of the Public Health Service Act” [42 U.S.C. 262 and 263b-263n and 21 CFR 50.3(j)]
**Clinical Trial** - a research study in which one or more human subjects are prospectively assigned to one or more interventions (which may include placebo or other control) to evaluate the effects of the interventions on biomedical or behavioral health related outcomes.

**Cognitively impaired** - having either a psychiatric disorder (e.g., psychosis, neurosis, personality or behavior disorders), and oHPAnic impairment (e.g., dementia) or a developmental disorder (e.g., mental retardation) that affects cognitive or emotional functions to the extent that capacity for judgment and reasoning is significantly diminished. Other disorders include persons under the influence of or dependent on drugs or alcohol and those suffering from degenerative diseases affecting the brain. Terminally ill patients, and persons with severally disabling physical handicaps, may also be compromised in their ability to make decision in their best interest.

**Confidentiality** – the ethical or legal right that information is considered private and will be held secret unless consent is provided permitting disclosure.

**Conflict of Interest** – a potential for a conflict of interest arises when PU or an individual holds a financial or associational Interest that may render, or create the appearance of rendering, PU or the individual incapable of making a decision that is in the best interests of PU, sponsors with whom PU has contracted with to perform certain clinical activities and of the individuals PU serves in its clinical and research activities. The mere existence of such an interest does not necessarily result in a conflict of interest. However, it is important that any such Interest is identified and evaluated before PU or other holder of the interest becomes involved in a decision or activity that could be biased by the interest.

**Continuing Noncompliance** – any noncompliance that occurs repeatedly to the point of suggesting a pattern or an underlying problem. Continuing noncompliance may occur due to lack of knowledge (unintentional) or due to deliberate choice to ignore regulations or determinations of the IRB (intentional).

**Covered Entity** - is the term applied to institutions that must comply with the Privacy Rule. These include:
- Health plans
- Health care clearinghouses
- Health care providers who conduct certain financial and administrative transactions electronically. These electronic transactions are those for which standards have been adopted by the Secretary under HIPAA, such as electronic billing and fund transfers.

**Data and Safety Monitoring Board** - A committee of scientists, physicians, statisticians, and others that analyzes data during the course of a clinical trial to monitor for adverse effects and other trends (such as an indication that one treatment is significantly better than another, particularly when one arm of the trial involves a placebo control) that would warrant modification or termination of the trial or notification of subjects about new information that
might affect their willingness to continue in the trial.

**Drugs** - include articles intended for use in the diagnosis, cure, mitigation, treatment, or prevention of disease and articles (other than food) intended to affect the structure or any function of the body of man or other animals [21 USC 321 SEC. 201]. Biologic products may be classified as drugs as well as certain cosmetics, nutritional supplements, and foods.

**Emergency Use** - is defined as the use of an investigational drug or biological product with a human subject in a life-threatening situation in which no standard acceptable treatment is available, and in which there is not sufficient time to obtain IRB approval.

**Engaged in Human Subjects Research** - An organization is considered engaged in human subjects research when its employees or agents, for the purposes of the nonexempt research project, obtain:

1. Data about the subjects of the research through intervention or interaction with them;
2. Identifiable private information about the subjects of the research;
3. The informed consent of human subjects for the research; or
4. When the institution receives a direct federal award to conduct human subject research, even when all activities involving human subjects are carried out by a subcontractor (that is, employees or agents of another institution). See Guidance on Engagement of Institutions in Human Subjects Research.

**Expedited Review** - review of proposed research by the IRB chair or an IRB member designee rather than by the entire IRB. Federal rules permit expedited review for certain kinds of research involving no more than minimal risk and for minor changes in approved research.

**Existing (Data, Documents, Records, Pathological or Diagnostic Specimens)** – Existing with regards to these materials means the items must be “on the shelf” or in existence at the time the project is submitted to the IRB for review.

**Federal Agency Other than DHHS that is subject to “The Common Rule” (45 CFR 46)**

Any one of the following:

1. Agency for International Development (22 CFR 225)
2. Central Intelligence Agency (Executive Order)
4. Department of Agriculture (7 CFR 1c)
5. Department of Commerce (15 CFR 27)
7. Department of Education (34 CFR 97)
8. Department of Energy (10 CFR 745)
10. Department of Justice (28 CFR 46)
11. Department of Transportation (49 CFR 11)
12. Department of Veterans Affairs (38 CFR 16)
13. Environmental Protection Agency (40 CFR 26)
14. Housing and Urban Development (24 CFR 60)
15. National Aeronautics and Space Administration (14 CFR 1230)
16. National Science Foundation (45 CFR 690)
17. Office of Science and Technology Policy (Adoption of policy)
18. Social Security Administration (Public law 7.5.26)

**Federal-Wide Assurance** - a formal written, binding commitment that is submitted to a federal agency in which an institution promises to comply with applicable regulations governing research with human subjects and stipulates the procedures through which compliance will be achieved.

**Guardian** – a person who is not the parent of a child, but who has been appointed by a court or juvenile court having jurisdiction over the child, to have a permanent self-sustaining relationship with the child and to make important decisions which have a permanent effect on the life and development of that child and to promote the general welfare of that child. A guardian may be a court or a juvenile court.

Unless otherwise enlarged or circumscribed by a court or juvenile court having jurisdiction over the child or by operation of law, the rights and duties of a guardian with respect to a child shall be as follows:

1. To consent to marriage, enlistment in the armed forces of the United States, or medical, psychiatric, or surgical treatment.
2. To serve as a guardian ad litem, unless the interests of the guardian conflict with the interests of the child or unless another person has been appointed guardian ad litem.
3. To serve as custodian, unless another person has been appointed custodian.
4. To make periodic visitations if the guardian does not have physical possession or custody of the child.
5. To consent to adoption and to make any other decision that the parents could have made when the parent-child relationship existed.
6. To make other decisions involving protection, education, and care and control of the child.

[From Iowa Code 232.2(21)]

**Human subject** –

*DHHS definition*: means a living individual about whom an investigator (whether professional or student) conducting research a) obtains information or biospecimens through intervention or interaction with the individual, and uses, studies, or analyzes the information or biospecimens; or b) obtains, uses, studies, analyzes, or generates identifiable private [From 45 CFR 46.102(e)]

*FDA definitions (human participant)*: an individual who is or becomes a participant in research, either as a recipient of the test article or as a control. A participant may be either a healthy human or a patient. [From 21 CFR 50.3(g)]
**Subject:** a human who participates in an investigation, either as an individual on whom or on whose specimen an investigational device is used or as a control. A subject may be in normal healthy or may have a medical condition. [From 21 CFR 812.3(p)]

**Humanitarian Use Device** - a device intended to benefit patients by treating or diagnosing a disease that affects fewer than 4,000 individuals in the United States per year.

**Identifiable Biospecimen** – a biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen. [From 45 CFR 46.102(6)]

**Identifiable Private Information** - private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information. [From 45 CFR 46.102(5)]

**Informed Consent** - 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. In giving informed consent, subjects may not waive or appear to waive any of their legal rights, or release or appear to release the investigator, the sponsor, the institution or agents thereof from liability for negligence.

**Institutional Review Board** - (IRB) means any board committee, or other group formally designated by an institution to review, approve the initiation of, and conduct periodic review of clinical research involving human subjects. The primary purpose of such review is to assure the protection of the rights and welfare of the human subjects.

**Interaction** - An interaction includes communication or interpersonal contact between investigator and participant.

**Intervention** - includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject’s environment that are performed for research purposes.

**Investigator** - in clinical trials, an individual who actually conducts an investigation. Any interventions (e.g., drugs) involved in the study are administered to subjects under the immediate direction of the investigator.

**Investigational New Drug or Device** - A drug or device permitted by FDA to be tested in humans but not yet determined to be safe and effective for a particular use in the general population and not yet licensed for marketing.

**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 procedure(s) involved in the research. If there is no applicable law addressing this issue, legally authorized representative means an individual recognized by institutional policy as acceptable for providing consent in the nonresearch context on behalf of the prospective subject to the subject’s participation in the procedure(s) involved in the research. [45 CFR 46.102 (i)]

In studies involving children in the state of Iowa, the LAR is:

1. the parent, OR
2. the court-appointed guardian.
In studies involving cognitively impaired adults in the state of Iowa, the LAR is:
1. the designated proxy (such as a Durable Power of Attorney for Health Care)
2. the court-appointed guardian
3. spouse
4. adult child
5. parent
6. adult sibling.

In studies that involve cognitively impaired adults, permission must be sought from the first existing person in the above lists, even if another relative is more conveniently available. Not reasonably available means the person is deceased, unknown, incompetent, or unable to provide permission due to inability to communicate with the research team (e.g., the individual is stationed outside the United States in the armed services and does not have access to phone, email, or fax).

**Limited Data Set** - is protected health information that excludes specific direct identifiers of the individual or of relatives, employees or household members of an individual. A limited data set can only be used for the purposes of research, public health, or healthcare operations, and disclosed for the purpose of research.

**Minimal risk** – the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests. [45 CFR 46.102(j) and 21 CFR 50.3(k)]

**In research involving prisoners** – the probability and magnitude of physical or psychological harm that is normally encountered in the daily lives, or in the routine medical, dental, or psychological examination of healthy persons. [45 CFR 46.303(d)]

**Minor change** – a change in the research plan that does not increase the risks or decrease the benefits related to the study (including risks related to procedures and methods, and to modifications that might negatively impact the statistical analysis of the research). If the change affects two of the following three aspects of the research, (i) the purpose, (ii) the population or (iii) the procedures; the change cannot be considered ‘minor’ and must be reviewed by the convened IRB unless the research itself is no greater than minimal risk and is limited to the categories of research eligible for expedited review.

**Noncompliance** – failure to follow the federal regulations with respect to protection of human subjects in research or failure to follow the determinations of the IRB with respect to conduct of the research as approved by the IRB.

**Nonscientist** - an individual who has little or no formal scientific or medical training or experience.
**Nonsignificant Risk (NSR) Device** – a device that does not meet the FDA definition for a significant risk device.

**Possibly Related to the Research** - There is a reasonable possibility that the adverse event, incident, experience or outcome may have been caused by the procedures involved in the research [modified from the definition of associated with use of the drug in FDA regulations at 21 CFR 312.32(a)].

**Principal Investigator** - The scientist or scholar with primary responsibility for the design and conduct of a research project.

**Prisoner** - any individual involuntarily confined or detained in a penal institution. This definition includes individuals sentenced to such an institution under a criminal or civil statute, individuals detained in other facilities by virtue of statutes or commitment procedures which provide alternatives to criminal prosecution or incarceration in a penal institution, and individuals detained pending arraignment, trial, or sentencing.

**Privacy** – freedom from unauthorized intrusion or the state of being let alone and able to keep certain personal information to oneself.

Private Information – includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record). [From 45 CFR 46.102(4)]

**Protected Health Information (PHI)** – is individually identifiable health information transmitted or maintained electronically or in any other form or medium, except for education records or employment records, as excluded in the Privacy Rule. [From 45 CFR 160.103]

If information includes protected health information, identifiable information includes any of the following information for the individual, relative, employer, or household member of the individual:

1. Names;
2. All geographic subdivisions smaller than a state, except for the initial three digits of the ZIP code if the geographic unit formed by combining all ZIP codes with the same three initial digits contains more than 20,000 people;
3. All elements of dates except year, and all ages over 89 or elements indicative of such age;
4. Telephone numbers;
5. Fax numbers;
6. Email addresses;
7. Social security numbers;
8. Medical record numbers;
9. Health plan beneficiary numbers;
10. Account numbers;
11. Certificate or license numbers;
12. Vehicle identifiers and license plate numbers;
13. Device identifiers and serial numbers;
14. URLs;
15. IP addresses;
16. Biometric identifiers;
17. Full-face photographs and any comparable images;
18. Any other unique, identifying characteristic or code, except as permitted for re-identification in the Privacy Rule.

Protocol - The formal design or plan of an experiment or research activity; specifically, the plan submitted to an IRB for review. 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.

Protocol Deviation - An intended or unintended modification of the procedures employed in the conduct of a research study that differs from the procedures in the IRB-approved protocol (excluding situations of emergency use). Protocol deviations that result in additional risks to subjects must be reported to the IRB.

Quorum – a majority of voting members of an IRB, including at least one member whose primary expertise is in a nonscientific area.

Research - a systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. The following activities are deemed not to be research:

(1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease
outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each federal agency) in support of intelligence, homeland security, defense, or other national security missions.

[From 45 CFR 46.102(l)]

The FDA defines research as a clinical investigation. Refer to the term “Clinical Investigation” in this section for the FDA definitions.

**Research Misconduct** – fabrication, falsification, plagiarism, or other practices that seriously deviate from those that are commonly accepted within the research community for proposing, conducting, or reporting research. It does not include honest error or honest differences in interpretations or judgments of data or creative innovations that are nonetheless ethical, legal and meet professional standards.

**Risk** – 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 may vary from minimal to significant.

**Serious Noncompliance** – Noncompliance that materially increases risks or that results in unexpected substantial harm to subjects or others. In addition the following instance(s) of noncompliance, as defined by OHRP, will always be determined as serious noncompliance:

1. Non-Exempt human subjects research being carried out without IRB review and approval or without appropriate informed consent.
2. Substantive modifications to IRB-approved research without IRB approval.

**Significant Financial Interest** - A significant interest consisting of one or more of the following interests of the Investigator (and those of the Investigator’s spouse and dependent children) that reasonably appears to be related to the Investigator’s institutional responsibilities:

1. With regard to any publicly traded entity, a Significant Financial Interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure and the value of any equity interest in the entity as of the date of disclosure,
when aggregated, exceeds $5,000. For purposes of this definition, remuneration includes salary and any payment for services not otherwise identified as salary (e.g., consulting fees, honoraria, paid authorship); equity interest includes any stock, stock option, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value;

2. With regard to any non-publicly traded entity, a Significant Financial Interest exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or when the Investigator (or the Investigator’s spouse or dependent children) holds any equity interest (e.g., stock, stock option, or other ownership interest); or

3. Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.

**Significant Risk (SR) Device** - a device that presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject. [From 21 CFR 812.3(m)]

**Suspension** - By requirement of the convened IRB or an IRB Chair, a temporary halt to a selection of research activities being conducted under an IRB approved project or a temporary halt to the IRB approved project as a whole. Suspended protocols remain open and require continuing review.

**Termination** - By requirement of the convened IRB, a permanent halt to some or all research activities in a previously approved IRB project. Terminated protocols are considered closed and no longer require continuing review.

**Test Article** – any drug for human use, biological product for human use, medical device for human use, human food additive, color additive, electronic product, or any other article subject to regulation under the Federal Food Drug and Cosmetic Act, or under sections 351 or 354-360F of the Public Health Service Act. [From 21 CFR 50.3(j) and 21 CFR 56.102(l)]

**Unanticipated Adverse Device Effect** – any serious adverse effect on health or safety or any life threatening problem or death caused by, associated with, a device, if that effect, problem or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application, or any other unanticipated serious problem associated with the device that relates to the rights, safety, or welfare of subjects [21 CFR 812.3(s)].

**Unanticipated Problem Involving Risk to Subjects or Others** – Any problem or event that:

1. was not expected given the nature of the research, the population under study and the approved procedures or protocol for conduct of the study,
2. is related to the research intervention, research procedures, and/or conduct of the research study, and
3. impacts the rights, safety, or welfare of subjects or others (e.g. those not directly involved in the research such as research staff or family members).

**Unexpected adverse event** - any adverse event occurring in one or more subjects participating in a research protocol, the nature, severity, or frequency of which is not consistent with either:

1. The known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol-related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or

2. The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject’s predisposing risk factor profile for the adverse event.

(Modified from the definition of unexpected adverse drug experience in FDA regulations at 21 CFR 312.32(a).)

**Voluntary** - Free of coercion, duress, or undue inducement. Used in the research context to refer to a subject’s decision to participate (or to continue to participate) in a research activity.

**Vulnerable Populations** – category of subjects who are vulnerable to coercion or undue influence, such as children, prisoners, individuals with impaired decision-making capacity, or economically or educationally disadvantaged persons.

**Written, or in writing** – refers to writing on a tangible medium (e.g., paper) or in an electronic format. [From 45 CFR 46.102(m)]
REVIEWED AND APPROVED BY: *(Signed document on file in HPA)*

PU-IRB Chair

_Date_

Parker Health System Chief Medical Officer

_Date_

__________________________________________________________________________________