Centra Health Institutional Review Board

STATEMENT OF COMPLIANCE
(USA)

Name of IRB: __Centra Health IRB________________________
IRB Address: __1901 Tate Springs Road____________________

__Lynchburg, VA 24501_____________________

Purpose:
The primary function of Centra’s Institutional Research Board (IRB) Committee is to safeguard the rights of all subjects at risk as the result of investigational activities supported and approved by the IRB of Centra Health, Inc. The IRB shall be responsible for reviewing, taking action on, and monitoring all proposed research activities conducted by the staff or other agents of Centra Health based on current federal, state or other regulations regarding investigational activities in human subjects.

Chairperson(s),
Dean Gianakos, MD, Chair
Amanda Keith, PharmD, BCPC, Vice Chair

List of Members, Terms

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<tr>
<td>Vicky Brunet, DNP, MSN Ed, NNP-BC, CCRN, Director Centra Nursing Research</td>
<td>Beth Burgess, IRB Secretary</td>
<td>Dean Gianakos, MD, Chair</td>
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<td>Sean M. Collins, Ph.D., CSCS*D, Community Member, Lynchburg College</td>
<td>Christina Delzingaro, MBA, CEO, Community Member, Free Clinic</td>
<td>Director Medical Student Education</td>
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<td>Frances Hill, RN, Staff Nurse and Lactation Consultant, Centra SCH</td>
<td>Michael A. Gillette, Ph.D., Centra Ethics Consultant</td>
<td>Amanda Keith, PharmD, BCPS, Vice Chair</td>
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<td>Holly B. Trent, Esq., Centra, General Counsel</td>
<td>Reverend Darren Miller, M.Div., BCC, Chaplain Coordinator, Spiritual Care and Education</td>
<td>Pharmacy – Clinical Specialist</td>
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<td>Donna J Washburn DNP, RN, CNS, ACNS-BC, AOCNS Clinical Nurse Specialist Centra Lynchburg Director Professional Clinical Practice</td>
<td>Christopher Lewis, MD, Cardiology, Administration</td>
<td>Tom Lawton, MBA, Centra– VP, Chief Resource Officer</td>
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<td>Jeff Wiggins, JD, MHA, CHC, CICA, Compliance Officer</td>
<td>Jenny Follett, MSN, NP-BC Sr. Clinical Research Coordinator</td>
<td>Ellen Morrison BSN, RN, MBA, CPHRM, Risk Manager, Centra</td>
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<td>Paul Bennett, MD, Community Member, Hospitalist</td>
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Selection of Members:
The Committee shall be composed of at least twelve (12) who are sufficiently qualified to execute the Committee’s charge based on experience and expertise. Members are expected to attend at least ten (10) Committee meetings each year. Members shall serve staggered terms of three (3) years with no maximum years of consecutive service.

The Nominating Committee will propose a slate of members to fill vacancies on the IRB Committee on an annual basis and as needed throughout the year. The

March 17, 2020
annual slate will be voted on by the IRB at its annual meeting and approved by the President/CEO of Centra. Recommendations from the Nominating Committee to fill vacancies other than the annual slate shall be voted on by the IRB, but do not require approval of the President/CEO.

Meetings:

The IRB Committee shall meet monthly on the third Tuesday of each month, which meeting may be rescheduled or cancelled at the discretion of the Chairperson. The annual meeting of the Committee shall be held on the third Tuesday in May, or at such other time as shall be determined by resolution. Special meetings may be called by the Chairperson or by at least twenty percent (20%) of the members of the Committee. A quorum for a meeting of the IRB shall be established when a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. A simple majority of those voting is sufficient for approval of any motion. Prior to each meeting, an agenda will be posted to the IRB Committee Webpage. Minutes of each Committee meeting shall also be posted on the Committee Webpage. The minutes shall include a list of all members in attendance, guests in attendance, and a summary of all actions and votes taken during the meeting.

Committees:

Executive Committee
Policy Committee
Nominating Committee
Exempt Committee
Ad Hoc Committees (as appointed by the Chairperson)
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I. HIPAA Authorization Form 1, Version 2 17MAR2020


N. AAMC Principles for Protecting Integrity in the Conduct and Reporting of Clinical Trials – January 6, 2006 (Anthem)
I. CHARGE TO THE BOARD

The Institutional Review Board (IRB) shall be charged with safeguarding the rights and welfare of Centra patients who are/or may potentially become subjects of investigational activities. Further, the IRB is available to review other investigational activities involving human subjects that are initiated elsewhere in the medical community. It is the responsibility of the IRB to review, take action on, and monitor all proposed research activities conducted by the staff or other agents of Centra Health, Inc. based on current federal or other regulations regarding investigational activities in human subjects. Relevant federal regulations are attached in the Appendices to this Manual. Further, the IRB also adopts the Institutional Review Board Guide Book OHRP IRB Guidebook prepared by the Federal Office for Protection from Research Risks as a resource to utilize in the conduct of its activities. This is located on the Centra IRB Member Education website. The IRB is responsible to the Chief Medical Officer of Centra Health, Inc. The IRB will keep minutes to the official IRB meetings available on the website https://centrahealth.sharepoint.com/sites/irb/default.aspx for the Board of Directors of Centra Health, Inc. and the Executive Committee of the Medical Staff at their request.

II. DEFINITIONS

“Office for Human Research Protections (OHRP)”—OHRP is a federal agency which provides leadership in the protection of the rights, welfare, and wellbeing of subjects involved in research conducted or supported by the U.S. Department of Health and Human Services (HHS). OHRP is part of the Office of the Assistant Secretary for Health (OASH) in the Office of the Secretary (OS), U.S. Department of Health and Human Services.

“Principal Investigator”—The local clinical expert or scientist primarily responsible for leading a particular clinical study.

“Significant Risk” Device Study—Under 21 CFR 812.3(m) an SR device means an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;

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1 Appendix J – also available https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=50&showFR=1
Appendix K – also available https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcfr/CFRSearch.cfm?CFRPart=56&showFR=1
Appendix L – also available https://www.hhs.gov/ohrp/sites/default/files/ohrp/policy/ohrpregulations.pdf

• Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
• Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
• Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

A NSR (Non-significant Risk) Device Study is one that does not meet the definition for a SR (Significant Risk) device study.³

III. MEMBERSHIP

The IRB shall be composed of at least (12) members who are sufficiently qualified to execute the Board’s charge based on experience, expertise and diversity of cultural and racial background. Both sexes and more than one profession shall be represented, and at least one member of the Board shall have no other affiliations with Centra Health, Inc.

In addition to possessing the professional competence necessary to review specific investigational activities, the IRB must be able to ascertain the acceptability of applications and proposals in terms of institutional commitments and regulations, applicable laws, standards of professional conduct and practice, and community attitudes. The IRB must, therefore, include at least one person who shall be a nonscientist and whose concerns are in these areas.⁴

The IRB may also appoint alternate members who may substitute at IRB meetings for absent IRB members provided the alternate’s qualifications are comparable to the absent member’s qualifications. Alternate members will have all the rights and access to committee materials as other members. Alternate members will only have voting privileges when they are attending meetings in the absence of the member for whom the alternate is substituting.

All IRB members, including alternates, shall be identified by name; earned degrees, if any; position or occupation; representative capacity; and by any other pertinent indications of experience such as Board certification, licenses, etc. sufficient to describe each member’s chief anticipated contribution to the IRB’s deliberations. Any change in IRB membership shall be reported to the Department of Health and Human Services in such form and at such times as the Secretary of the DHHS may require. IRB membership is recorded on a roster that is submitted to the federal Office for Human Research Protections (OHRP).⁵

⁴ Reference 21 CFR 56.107(c)
⁵ Appendix A
Annually, and whenever a member’s interest changes, all IRB members must review and sign the “Centra Institutional Review Board Conflicts of Interest Disclosure Form for IRB Members”. The IRB Chairperson shall review all members’ Conflicts of Interest Disclosure Forms upon receipt. In the event the Chairperson identifies a potential Conflict of Interest, he may establish an Ad Hoc IRB Conflict of Interest Committee comprised of at least four (4) IRB members to review and make recommendations to the IRB Board as to management of potential conflicts. The Committee will consider whether an actual Conflict of Interest exists, and if so, methods for managing the Conflict of Interest. These may include:

A. public disclosure of “financial interests;”

B. divestiture of significant financial interests;

C. severance of relationships that create actual or potential conflicts;

D. requiring the conflicted Member to leave the room during discussion and voting on the approval of the research.

The Conflict of Interest Committee will make its recommendations to the full IRB for resolution. The Board will determine by majority vote whether the Committee’s recommendations provide appropriate safeguards to protect Centra patients and human subjects. If so, a Management Plan will be developed and provided to the individual with the conflict and the Plan will be monitored to ensure compliance by the Conflict of Interest Committee. Whether or not disclosed on an IRB member COI Disclose Form, any Board Member who believes he/she may have a Conflict of Interest with respect to proposed research shall refrain from voting on any matter relating to the study, and he/she may not be present during the final consideration of the application for approval of the research.

Terms. Members will serve staggered terms of three years with no maximum years of consecutive service.

Selection of Members. The Nominating Committee will propose a slate of members to fill Board membership on an annual basis. The annual slate will be voted on by the Board at its annual meeting and approved by the Chief Medical Officer of Centra.

IV. MEETINGS

Regular Meetings. The IRB shall meet monthly on the third Tuesday of each month, which meeting may be rescheduled or cancelled at the discretion of the Chairperson.

Annual Meeting. The annual meeting of the IRB shall be held on the third Tuesday in May, or at such other time as shall be determined by resolution of the Board.

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6 Appendix B; Reference 21CFR.56.107d
7 VIII.C. of this manual
Special Meetings. Special meetings of the Board may be called by the Chairperson or by at least twenty percent (20%) of the members of the Board.

Quorum. A quorum for a meeting of the IRB shall be a meeting at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. A simple majority of those voting is sufficient for approval of any motion (including, but not limited to, approval of minutes, studies, and amendments to policies and procedures).

Attendance. Members of the Board are expected to attend. Failure to attend may lead to a request by the Board for the member’s resignation.

V. OFFICERS

The IRB officers include, but are not limited to: Chairperson, Vice Chair and Secretary. The President/CEO of Centra shall appoint the IRB Officers on an annual basis prior to the IRB annual meeting.

General Duties of Officers. Each of the Officers shall undertake to provide leadership to the IRB. The Chairperson shall be responsible for chairing each of the IRB meetings. In his/her absence, the Vice Chair shall be responsible for chairing such meetings. The Secretary shall be responsible for recording minutes at each IRB meeting, and such other duties as the Chairperson may assign.

VI. IRB RECORD KEEPING

A. The following documentation of the IRB activities will be prepared and maintained (electronic format is acceptable):
   1. Investigational activity proposals including consent forms.
   2. Minutes of meetings.
   3. Records of continuing review.
   4. Copies of correspondence between the IRB and investigators.
   5. A list of IRB members
   6. Written policies and procedures of the IRB.

B. Such documentation for a given study will be maintained for at least three years after completion of the study.  

VII. IRB MINUTES

The minutes of the IRB meetings shall include the following:
   A. List of members in attendance, members absent, and guest(s) in attendance.
   B. Actions.
   C. Basis for requiring changes in disapproved investigational activity proposals.
   D. A written summary of the discussion of controversial issues and their resolution.

VIII. IRB COMMITTEES

8 21CFR §56.115(b)
A. The Executive Committee is a standing committee that meets as needed regarding issues that may arise that require the IRB to take immediate action in between meetings. Members include:
   1. Chair of the IRB
   2. Vice Chair of the IRB
   3. Secretary of the IRB
   4. Compliance Officer/General Counsel
All actions taken by the Executive Committee will be reported to the full IRB at its next meeting.

B. The Policy Committee is a standing committee that meets at least annually and as needed to review and revise the IRB policies and procedures manual. The committee makes recommendations to the full IRB. The IRB considers the recommendation(s) and may approve with a majority vote. The Committee is composed of the following members:
   1. Chairperson of the IRB, or the Vice Chair of the IRB in the Chair’s absence.
   2. Secretary of the IRB
   3. Compliance Officer or General Counsel
   4. Scientific/Clinician Member of the IRB
   5. Two Other IRB Members
All actions taken by the Policy Committee will be reported to the full IRB at its next meeting.

C. The Nominating Committee is a standing committee that meets at least annually and as needed to solicit and review nominations for new Board members. Nominations for new Board members will be accepted by the Nominating Committee from Board members, peers, and other appropriate leaders within Centra, and candidates will be identified and selected by the Nominating Committee based on criteria for competency. Members include:
   1. Executive Committee members
   2. One other IRB member
All actions taken by the Nominating Committee will be reported to the full IRB at its next meeting.

D. The Exempt Committee is a standing committee of at least two IRB members appointed by the Chairperson of the IRB for purposes of reviewing and evaluating Exempt Research Checklists and confirming that an Application for IRB approval is not required.
All actions taken by the Exempt Committee will be reported to the full IRB at its next meeting.

E. Ad-Hoc Committees: At times, the Chairperson of the IRB may appoint ad-hoc committees to consider special items and make recommendations to the Chairperson and/or the IRB. All actions taken by all Ad-Hoc Committees will be reported to the full IRB at its next meeting.
IX. RELATIONSHIP OF THE IRB TO OTHER COMMITTEES

Any research proposal involving human subjects which will involve the exposure of the patient or medical personnel to an amount of radiation in excess of what they would receive during a routine examination in radiology or nuclear medicine, must be submitted to the Radiation Safety and Medical Isotopes Committee for approval prior to action by the IRB. In involving the use of x-rays or radioisotopes, the IRB will inform the Radiation Safety and Medical Isotopes Committee of its actions by providing copies of the minutes of their meetings. 9

X. PROCESSING OF APPLICATIONS AND REVIEWER RESPONSIBILITIES

All research involving human subjects conducted, supported, or otherwise subject to regulation by any federal department or agency will be subject to IRB review. All Investigators are required to complete an application applicable to the status of the study. All proposals for investigational activities must be submitted to the IRB at least fourteen (14) days prior to the next meeting for consideration and possible action at that meeting. In general, action on all proposals will be taken within six (6) weeks after submission.

Centra Institutional Review Board Conflict of Interest Questions and Certification is required from each Principal Investigator at least annually or if Principal Investigator changes. This form is included in the:

- “Application for IRB approval of Human Subjects Research Form 1” 10
- “Request for Renewal/Update of IRB Approval Form 2A or Study Closure Form 2B” 11
- “Modification of Approved Human Subjects Research Form 3” 12

IRB members shall review and consider Principal Investigator’s Conflict of Interest Questions and Certification Forms. In the event any Member identifies a potential Conflict of Interest, he shall bring it to the attention of the Chairperson, and the Chairperson may establish an Ad Hoc IRB Conflict of Interest Committee comprised of at least four (4) IRB members to review all Conflicts of Interest reported by Principal Investigators on the IRB Conflict of Interest Questions and Certification form. The Committee shall make recommendations to the IRB Board as to management of potential conflicts. The Committee will consider whether an actual Conflict of Interest exists and if so, methods for managing the Conflicts of Interest. These may include:

- Public disclosure of “financial interests;”
- Monitoring of research by independent, external reviews;

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9 Refer to Appendix C, Form 1, Part A.2.15
10 Appendix C
11 Appendix D
12 Appendix E
• Modification of the research plan;
• Disqualification from participation in all or part of the research;
• Divestiture of Significant Financial Interests;
• Severance of relationship that create actual or potential conflicts.

The Conflict of Interest Committee will make its recommendations to the full IRB Board for resolution. The Board will determine by majority vote whether the Committee’s recommendation provides appropriate safeguards to protect Centra patients and human subjects. If so, a Management Plan will be developed and provided to the individual with the conflict and the Management Plan will be monitored to ensure compliance by the Conflict of Interest Committee. Non-compliance with the Management Plan shall be grounds for terminating the study.

The IRB will make a risk determination at the meeting for initial device approval when the sponsor presents a device for investigation as Non-Significant Risk (NSR). Unless the FDA has already made a risk determination for the investigation, the IRB will review the sponsor’s NSR determination for each investigational device study reviewed. If the IRB determines that an investigation involves a significant risk device, presented by the sponsor as NSR, the IRB will notify the investigator and the sponsor of the SR determination.13

A letter of decision will be sent by the IRB Chairperson to the Principal Investigator and the study coordinator within five (5) business days of the IRB’s vote. The letter shall contain the following:

• Date of decision
• Expiration Date of approval and requirements for renewal(s)
• Explanation of IRB general expectations and any specific requirements
• If a device study, designation of whether the device study is deemed “significant risk” or “non-significant risk”

A. Initial Approval:

1. The Principal Investigator will complete an “Application for IRB approval of Human Subjects Research Form 1.” 14 His/Her credentials are to be included in the submission.

2. The Investigator may consult with the Chairperson of the IRB regarding the formation of a Special Resource Committee15, which will be composed of at least one person qualified to review this investigational activity.
   a. The Chairperson will decide if this proposal must go to a Special Resource Committee or directly to the IRB. If the Proposed investigational activity must go to a Special Resource Committee, the Chairperson of the IRB will appoint the Committee and provide copies of the proposal to the Special Resource Committee Chairperson.

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14 Appendix C
15 See VIII.e.
b. This Committee will recommend either approval or disapproval of the proposed investigational activity. The proposed investigational activity application and the Committee’s recommendation shall be forwarded to the Chairperson of the IRB by the Committee.

3. All proposed investigational activities must have the necessary pre-approvals completed and submitted electronically to the Chairperson of the IRB before the next scheduled meeting of the full Board. The Chairperson of the IRB is responsible for development and distribution of meeting agendas.

4. The Principal Investigator/Sub-Investigator/Study Coordinator will be asked to appear at the IRB meeting to present their research application and answer any questions about the proposed investigational activity as it pertains to the protection of the rights and welfare of the research subjects.

5. IRB approvals are a period of (1) year, or such other period as determined by the IRB. Approximately thirty (30) days prior to the end of the approval period, the IRB Chairperson will provide in written or electronic notice to the Principal Investigator the following:
   a. the date the study is due to expire,
   b. the date (two weeks prior to the upcoming meeting) the applicable application must be submitted to the Secretary of the IRB, and
   c. the anticipated IRB review date. The investigation may not continue if not approved by the IRB prior to the end of the initial or annual approval period. The Principal Investigator or a Study Coordinator will need to be available either in person or by phone as directed by the IRB Secretary and the IRB Chairman.

B. Other applications include:
   1. Request for Renewal of IRB Approval, Form 2A or Study Closure, Form 2B.16
   2. Modification of Approved Human Subjects Research, Form 3.17 Modifications include changes or additions to the study protocol or informed consent form, change of Principal Investigator.
   3. Reports of Approved Human Subjects Research Form 4.18
   4. Protected Health Information: Waiver of Authorization to Perform Human Subjects Research, Form 5.19
   5. Exempt Research Checklist, Form 6.20
   6. HIPAA Authorization, Form 7.21

XI. Other Categories of Review or Reviewers Responsibilities

16 Appendix D
17 Appendix E
18 Appendix F
19 Appendix G
20 Appendix H
21 Appendix I
A. **Emergency Use** – “Emergency use means the use of a test article on 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.” 22

The emergency use of an unapproved investigational drug or biologic requires an Investigation New Drug (IND). 23 If the intended subject does not meet the criteria of an existing study protocol, or if an approved study protocol does not exist, the usual procedure is to contact the manufacturer and determine if the drug or biologic can be made available for the emergency use under the company’s IND. The need for an investigational drug or biologic may arise in an emergency situation that does not allow time for submission of an IND. In such a case, FDA may authorize shipment of the test article for a specialized use in advance of the IND submission. Requests for such authorization may be made by telephone or other rapid communication means. 24 A similar process is applicable to use experimental devices. 25

Emergency use of a test article is exempt from IRB requirements, provided that such emergency use is reported to the IRB within five (5) working days and any subsequent use of the test article at the institution is subject to IRB review. FDA regulations require that any subsequent use of the investigational product at the institution have prospective IRB review and approval. FDA acknowledges, however, that it would be inappropriate to deny emergency treatment to a second individual if the only obstacle is that the IRB has not had sufficient time to convene a meeting to review the issue.

B. **Expedited Review:**
In some cases, the Chairman and Vice Chairman may review and unanimously agree to approve an application to renew. If the criteria for expedited review are not met, or if there is not agreement to approve the application, the application must be reviewed by the full board.

The requirements for approval of an application for expedited review of a renewal are as follows:

1. The research is permanently closed to the enrollment of new subjects
2. All subjects have completed all research-related intervention
3. The research remains active only for the purpose of long term follow-up
4. No subjects have been enrolled since the last approval and no additional risks have been identified and
5. The remaining research activities are limited to data analysis

All new applications for research involving human subjects are reviewed by the full board.

C. **Waiver of Jurisdiction**

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22 CFR 56.102(d)
23 21 CFR. Part 312
24 21 CFR. § 312.36
25 21 CFR. Part 812
Local investigators may request a waiver of jurisdiction to another IRB. The investigator seeking a waiver from Centra’s IRB should send a letter, or email, to the IRB secretary and should include the following documents:

1. The application that was made to the IRB of record providing review
2. The study protocol
3. The informed consent
4. A description of the IRB providing review
   Note: A link to a website is sufficient if it provides enough information for the Centra IRB to evaluate.
5. An authorization agreement that delineates the responsibilities of each party, as applicable.

If the investigator provides the documentation referenced above, a Centra IRB application is not required.

Investigators who participate in waived investigations are encouraged to report the following information for each study to the IRB annually:

1. Annual total and local enrollment (number of subjects enrolled)
2. Local SAEs reportable to the IRB of record
3. Local protocol deviations and/or violations reportable to the IRB of record

The Centra IRB may approve the use of another IRB in cases where an academic institution allows a local investigator to enroll Centra patients but will not otherwise provide a reliance agreement to the Centra IRB. This is not a “waived” study per se, and the IRB at the institution has no responsibility to the Centra IRB. However, the local investigator continues to be responsible for reporting to the Centra IRB and the Centra IRB will have the authority to discontinue local enrollment. The local investigator will be encouraged to report the same information as other investigators who report on waived studies.

D. Lapsed Studies
All studies expire at midnight on the expiration date. Once the approval period for a given study has expired without renewal it is considered a lapsed study and investigators must stop all research activities involving human subjects except where doing so would jeopardize the welfare of the subject. All enrollments must cease along with continuation of research interventions or interactions with currently participating subjects and data analysis of identifiable private information.

The IRB Chairperson will send a written notice within two (2) days of the lapse notifying the principal investigator that the IRB approval has expired.

When a protocol is lapsed, the Investigator must stop all activity on the protocol, including subject recruitment and enrollment, procedures, and analysis and/or publication of existing data.
If withdrawal of current participants from the research is necessary, the Investigator will be required to:

A. Inform enrolled participants that the study has lapsed; and
B. Develop procedures for withdrawal that protect the rights, safety, and welfare of participants, and describe those procedures to participants.

The Principal Investigator may apply for a renewal following the lapse and the IRB will review the application at the next meeting. If approved, the study may resume. The IRB cannot retrospectively grant approval to cover a period of lapsed IRB approval.

E. Suspension or Termination of a Study by the IRB

Definitions:
Suspension: All project activities must cease until any pending issues can be resolved satisfactorily. Suspended studies are still approved, but in a ‘hold’ status until the pending issues can be resolved.
Termination: The study is no longer approved. All project activities must cease immediately, including data analysis and any resulting data or analysis is null and void. A study may be terminated by the IRB or by the sponsor for administrative, regulatory or other reasons (such as initial study results). Regardless of the reason, terminated studies are not considered completed.
Closure: This is an administrative status whereby a previously approved protocol’s expiration date has passed and an investigator has not submitted a renewal, or the investigator has submitted a study closure request. The IRB assumes that no human subject research activities are ongoing and, for administrative record keeping, the study record is closed.

The IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with federal and state regulations, IRB requirements, or research that has been associated with unexpected serious harm to subjects (45 CFR 46.113). A research project may be suspended or terminated for a variety of reasons, including but not limited to:

1. Serious adverse event(s) and unanticipated problem(s)
2. Detrimental change in the risk-benefit ratio of the study
3. Conduct of research activities without prior IRB approval
4. Failure to obtain appropriate consent
5. Failure of investigators to complete required training
6. Other noncompliance issues

Upon termination of a study, the IRB Chairperson shall include a statement of the reasons for the IRB’s action and promptly report the termination to the OHRP, the regional office of the FDA, and other regulatory bodies as indicated. The report will give the reasons for termination and the effective date.

Suspension and termination process and notification:
- When potential cause for further investigation is demonstrated, an inquiry into the specific circumstances giving rise to concern with a specific protocol will be conducted. If a protocol is determined not be in noncompliance or a
detrimental change in the risk/benefit occurs, further action will be taken by
the IRB.

- In most cases, the IRB will review the circumstances of the case and make
  a determination of suspension or need for termination. Other IRB members
  may be consulted as needed in the decision making process leading up to
  bringing the issue to the full committee.

- In emergency situations, the IRB Chair in consultation with the IRB Vice
  Chair, will make a determination of the need to suspend or terminate a study
  immediately.

- The IRB Chair (or his or her designee) will write a letter that includes the
  following:
    1. A description of the event
    2. The determination of the IRB (i.e. suspension, termination)
    3. Justification for the determination
    4. Requirements of the investigator (e.g. cease all data collection)

The letter will be forwarded to the Investigator, any Sponsor(s), and
applicable federal agencies (E.g. FDA, OHRP-Office for Human Research
Protection). A copy of the form is filed with the protocol’s IRB file.

- The Lead Investigator is responsible of notifying (in a timely manner) all co-
  investigators, key personnel, and other research staff associated with the
  protocol as well as any subcontract grantees if the protocol has been
  suspended or terminated.

**Participant Involvement in Suspended or Terminated Protocols**

When a protocol is suspended or terminated, the Investigator must stop all activity
on the protocol, including subject recruitment and enrollment, procedures, and
analysis and/or publication of exiting data.

When the suspension or termination of a research protocol involves the withdrawal
of current participants from the research, the Investigator will be required to:

1. Inform enrolled participants that the study has been suspended or
   terminated; and

2. Develop procedures for withdrawal that protect the rights, safety, and
   welfare of participants, and describe those procedures to participants.

In certain circumstances, project activities may continue if stopping study
procedures/treatment will adversely affect the welfare of a subject. If the
suspension or termination of a research protocol does involve the withdrawal of
current participants from the research, the Investigator will be required to:

1. Notify the OHRP immediately of the need to continue any procedures/
   treatment;

2. Inform enrolled participants that the study has been suspended or
   terminated; and,

3. Report any serious adverse events or unanticipated problems involving
   risks to participants to the IRB.

**Reinstatement of Suspended or Terminated Protocols**
**Suspended Studies:** To reinstate a project that has been suspended, the investigator must resolve satisfactorily any pending issues as required by the IRB. After one year of suspension or the expiration date of the study (whichever comes first), if adequate progress has not been made on the pending issues then the IRB will administratively close the study protocol.

To reinstate a project that has been suspended the investigator must contact the OPHS in writing within 30 days of the suspension. The investigator must address the following in a letter:

1. Reason for requesting the study be reinstated.
2. Short summary of the purpose of the study and intended objectives/outcomes. This may be incorporated into the protocol narrative noting any changes, revisions or clarification.
3. Description of how the study has changed, if any, since initial approval using the appropriate Amendment form and procedure for identifying changes in the protocol narrative.
4. Summary of status of the study, including:
   a. How many subjects were enrolled;
   b. At what point in the treatment/procedures were the subjects at the time of suspension;
   c. Any adverse events or amendments since last continuing review, including a description of each;
   d. Any additional relevant information.
5. Documented plan to ensure that reason for suspension will not happen again and that the study will be in compliance with all applicable laws and regulations.
6. Anticipated enrollment, if the study is reactivated.
7. In the case that IRB-approval of a protocol is reinstated, the IRB may require that subjects who were previously enrolled be re-consented.

**Terminated Studies.** Terminated studies may be reinstated or reactivated with appropriate modifications to address the reason(s) the study was terminated. Investigators will need to submit a completely new application if they wish to resume a terminated study.

F. **Exempt**

Exempt Research Checklist (Form 6) will be submitted to the Exempt Committee for consideration and confirmation that an application to the IRB is not required. If not determined as Exempt, an Initial Application (Form 1) will need to be submitted.26

G. **Miscellaneous**

For requests not otherwise defined above, the IRB Board has the authority to meet and consider such requests at the discretion of the Chairperson.

XII. **INFORMED CONSENT**

The IRB shall be charged with the safeguarding of the rights and welfare of subjects at risk in investigational activities supported by the IRB of Centra Health, Inc. No

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26 See X.A. and Appendix C of this manual
investigational activity involving human subjects shall be undertaken unless the IRB has reviewed and approved such investigational activity. This review will evaluate the relative risks and benefits and will require a legally effective informed consent as outlined by both the FDA and the HHS to be obtained and documented. Specific attention should be paid to Guidelines for Informed Consent as contained in federal regulations. Specific attention should be given to paragraph 21 CFR Section 50.25 which outlines the elements of informed consent.

A. In seeking informed consent, the following information shall be provided to each subject:

1. A statement that the study involves research, an explanation of the purposes of the research and the duration of the subject’s participation, a description of the procedures to be followed, and identification of any procedures which are experimental.
2. A description of any reasonably foreseeable risks or discomforts to the subject.
3. A description of any benefits to the subject or to others which may reasonably be expected from the research.
4. A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject.
5. A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained and that notes the possibility that the Food and Drug Administration may inspect the records.
6. For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained.
7. An explanation of whom to contact for answers to pertinent questions about the research and research subjects’ rights, and whom to contact in the event of a research-related injury to the subject.
8. A statement that participation is voluntary, that refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and that the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.

B. Additional elements of informed consent: When appropriate, one or more of the following elements of information shall also be provided to each subject:

1. A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable.
2. Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent.
3. Any additional costs to the subject that may result from participation in the research.
4. The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject.

21 CFR Section 50.25
5. A statement that significant new findings developed during the course of the research which may relate to the subject’s willingness to continue participation
6. The approximate number of subjects involved in the study.

C. When seeking informed consent for applicable clinical trials, as defined in 42 U.S.C. 282(j) (1) (A), the following statement shall be provided to each clinical trial subject in informed consent documents and processes. This will notify the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (j) of section 402 of the Public Health Service Act. The statement is: “A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this web site at any time.”

D. Consent process:

1. No investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative.
2. An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.
3. The information that is given to the subject or representative shall be in language understandable to the subject or the representative.
4. No informed consent, whether oral or written, may include any exculpatory language through which the subject or the representative 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.

E. Vulnerable population include:

1. Pregnant Females and Fetuses – Because of the inherent danger to fetuses of some investigational activities, use of women to child-bearing age or women known to be pregnant is specifically discouraged, unless it is clearly evident that no potential danger to the fetus exists. The Principal Investigator shall make it his responsibility to inform the research subjects that they should not become pregnant during the research project and should they become pregnant they will be eliminated from the study.
2. Prisoners – Investigational activities using prisoners must be in compliance with both FDA and HHS regulations. Any investigational activity involving prisoners will necessitate a review by a Special IRB which includes a prisoner advocate. This IRB will be constituted of the regular Centra Health, Incorporated IRB plus the prisoner advocate.
3. Children and the Individuals with Mental Disabilities – The use of children (subjects less than 18 years of age) or those who are individuals with mental disabilities (subjects whose mental age is less than 18 years) is discouraged unless there are no reasonable alternatives. It is recommended that investigators consider the use of adults or animals in preference to children whenever possible.
All investigational activities using subjects less than legal age will require informed consent from the parents or guardians of the subject children. Individuals with mental disabilities must have informed consent obtained from parents or legal guardians, and in the case where parents are unavailable such as in the situation where the subject is in foster care or in another institutional setting, there will be an officially designated representative for the individuals with mental disabilities. In situations where the mental age is greater than 12 years (subjects who are either individual with mental disabilities disabled or minor children) the assent of the subject will also be obtained in addition to the informed consent and permission of the parent or guardian. If the investigational activity presents substantial risk to the subjects and there is substantial reason to believe that the parents or legal guardians of investigational activity subjects may be unable to consider adequately their child or ward’s interest in determining whether to consent to participate in the investigational activity, an advocate shall be appointed to review the case of each child and to decide whether it is in the child’s interest to participate. If an advocate is appointed, his or her consent must be obtained as well as that of the parent or guardian and the subject (where applicable).

XIII. CRITERIA FOR DENYING APPROVAL

The IRB may deny any proposed research activity consistent with its policies and procedures upon review, including but not limited to studies for which the following conditions apply:

A. The proposed research activity violates laws or regulations established by the Federal Government, the Commonwealth of Virginia or Centra Health, Incorporated.

B. If, in the judgment of the IRB, the risk created to the subjects outweighs the benefits to be obtained.

C. If, in the process of conducting an investigational activity, unnecessary risks are imposed, the investigational activity will be disapproved. In this regard, it is expected that all investigational activities involving human subjects will attempt to minimize the amount of risk imposed as outlined in the federal regulations.

D. In the IRB’s judgment there is insufficient Informed Consent.

E. The IRB judges that payment or other offered inducements are likely to unduly influence subjects and/or investigators.

XIV. COMPLIANCE

Definitions:

*Non-compliance* – non-compliance with the regulations or the requirements of determinations of the IRB.

*Serious Non-compliance* – Any non-compliance that results in harm to subjects, or poses a risk of harm to subjects. Examples include conducting human subjects research without IRB approval; failure to obtain informed consent prior to a participant’s involvement in research.
**Continuing Non-compliance** – Any event that in singular does not constitute non-compliance, but in aggregate does. Examples include a PI misses a continuing review deadline three years in a row; a PI has multiple studies with the IRB and misses more than three deadlines.

It is the responsibility of the IRB to monitor compliance with protocols for investigational activities to protect the rights of human subjects and ensure compliance with the requirements and determinations of the IRB.

Non-compliance may be discovered in a number of ways, including investigator monitoring, complaints, protocol deviations, and reports by PIs to the Board. All concerns about non-compliance should be reported to any member of the IRB who will report the information to the IRB Chair. Reports of non-compliance may be made by email, telephone or in person. Anytime the IRB becomes aware of possible non-compliance and determines that an investigation is warranted, the IRB Chair may appoint a subcommittee to review the allegations of non-compliance and conduct an investigation. The subcommittee will meet, collect information about the allegations of non-compliance, triage the information, and determine whether non-compliance occurred. If non-compliance occurred, the subcommittee will also consider and determine whether the non-compliance is serious or continuing. If the subcommittee determines that non-compliance has occurred but it was neither serious nor continuing, the subcommittee will recommend steps to be taken to address the issue and prevent such non-compliance in the future. If the subcommittee determines serious or continuing non-compliance has occurred, the information will be presented to the IRB for discussion and final determination as to what action is appropriate.

Once the IRB has heard the subcommittee’s report, it will discuss and determine next steps. The IRB may take any number of actions in response to reports of non-compliance, keeping in mind that its duty is to protect human research subjects. Actions which may be taken by the IRB include, but are not limited to, educating the investigator and/or research staff, suspending or terminating the research, suspending the investigator, notifying participants, modifying the protocol and/or consent, monitoring the research, requiring continuing review more frequently than once a year, conducting random audits of the investigator, and modifying or suspending other protocols in the event the non-compliant PI has more than one study.

Anytime the IRB makes a determination of serious or continuing non-compliance, the IRB Chair will report such non-compliance to the ORHP or the FDA by summarizing the investigation and basis for the determination, and submitting that summary in writing within 30 days of the IRB’s determination, or sooner as required given the circumstances.

For serious or continuing noncompliance, reports to regulatory agencies will include:
A. Name of the institution conducting the research;
B. Title of the research project in which the noncompliance occurred, or for IRB or institutional noncompliance, the IRB or institution involved;
C. Name of the principal investigator on the protocol;
D. Number of the research project assigned by the IRB and the number of any applicable federal award(s);
E. A detailed description of the noncompliance;
F. Actions the institution is taking or plans to take to address the noncompliance.

INVESTIGATOR COMPLIANCE

It is the responsibility of the IRB to monitor compliance with protocols for investigational activities to protect the rights of human subjects. It will be the responsibility of the IRB to recommend the frequency and method for monitoring all investigational activities to assure investigator compliance. Such monitoring will focus specifically on changes in study protocol and obtaining and documenting informed consent. At the time of approval of an investigational activity, the IRB will establish a schedule for conducting continuing review of the research and investigational activities that are the subject of the approval. Such reviews will be scheduled to occur and must occur no less frequently than annually.

Monitoring and documenting investigator compliance falls into three major categories:

A. Business monitoring to be accomplished by submission of the annual renewal application assuring no changes in protocol or untoward effects occurring within human subjects.

B. Interim reports to the IRB will be made during the course of the investigational activity, as required by law, documenting any changes in the protocol or any unanticipated events occurring in a human subject. Interim reports must be made in writing at the time of occurrence to the Chairperson of the IRB or his/her designee. Copies of the report shall be distributed to all IRB members and kept on file. Changes to any protocol cannot be initiated without the approval of the IRB.

C. Reviews will be scheduled at more frequent intervals than annually if the IRB determines that the degree of risk of the approved research and investigational activity warrants such more frequent review. Special monitoring procedures for high risk or other projects as deemed necessary by the IRB which will be determined at the time of approval. Specific mechanisms for monitoring both informed consent and protocol adherence will note the frequency and method by which monitoring is to be accomplished and the individual(s) who is/are responsible for such monitoring activities.

XV. REPORTING OF UNANTICIPATED PROBLEMS AND ADVERSE EVENTS TO THE IRB

Federal regulations require investigators to report to the IRB any unanticipated problems involving risks to subjects or others. It is important to understand the difference between “adverse events” and “unanticipated problems” because many adverse events are not reportable.

A. “Adverse event” or “adverse experience” is 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, temporarily associated with the subject’s participation in the research, whether or
not considered related to the subject’s participation in the research. Adverse events encompass both physical and psychological harms and occur most frequently in the context of biomedical research, although they can occur in the context of social and behavioral research.

B. “Serious Adverse Event” (SAE) is any adverse event associated with the subject’s participation in research that meets any of the following criteria:

1. results in death;
2. is life-threatening (places the subject at immediate risk of death from the event as it occurred);
3. requires hospitalization or prolongation of existing hospitalization;
4. results in persistent or significant disability/incapacity;
5. results in a congenital anomaly/birth defect;
6. any other adverse event that, 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 (examples of such events include allergic bronchospasm requiring intensive treatment in the emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse).

C. “Unexpected Adverse Event” is any adverse event, the specificity or severity of which is not consistent with the current investigators brochure; or, if an investigator brochure is not required or available, the specificity or severity of which is not consistent with the risk information described in the general investigational plan or elsewhere in the current research application, as amended.

D. “Unanticipated Problem” (UP) The phrase “unanticipated problems involving risks to subjects or others” is found but not defined in the federal regulations at 45 CFR part 46. Federal guidance considers unanticipated problems, in general, to include any incident, experience, or outcome that meets all of the following criteria:

1. 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;
2. related or possibly related to participation in the research (in this guidance document, 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

3. 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.

Federal guidance recognizes that it may be difficult to determine whether a
particular incident, experience, or outcome is unexpected and whether it is
related or possibly related to participation in the research. It notes that an
incident, experience, or outcome that meets the three criteria above generally will
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. Examples of corrective
actions or substantive changes that might need to be considered in response to an
unanticipated problem include:

1. changes to the research protocol initiated by the investigator prior to
obtaining IRB approval to eliminate apparent immediate hazards to
subjects;

2. modification of inclusion or exclusion criteria to mitigate the newly
identified risks;

3. implementation of additional procedures for monitoring subjects;

4. suspension of enrollment of new subjects;

5. suspension of research procedures in currently enrolled subjects;

6. modification of informed consent documents to include a description of
newly recognized risks; and

7. provision of additional information about newly recognized risks to
previously enrolled subjects.

E. Investigators must report SAEs and UPs to the IRB within five (5) business days
of knowledge of the event from the sponsor. Reports must be made to the IRB. The
report to the IRB must include the name of the research project in which the
reportable incident occurred; name of the principal investigator on the protocol;
number of the research project assigned by the IRB and the number of any
applicable federal award(s) (grant, contract, or cooperative agreement) if any; a
detailed description of the problem; and actions proposed or being taken or
planned to be taken to address the reportable incident (e.g., revise the protocol,
suspend subject enrollment, terminate the research, revise the informed consent
document, inform enrolled subjects, increase monitoring of subjects, etc.), and
confirmation that the event has been reported in accordance with section XV. 29
of this manual.

29 Section XV. of this manual
F. Investigators must report local SAEs and UPs to the IRB within five (5) business days of knowledge of the event. Reports must be made to the IRB Chairperson. The report to the IRB must include the name of the research project in which the reportable incident occurred; name of the principal investigator on the protocol; number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement) if any; a detailed description of the problem; and actions proposed or being taken or planned to be taken to address the reportable incident (e.g., revise the protocol, suspend subject enrollment, terminate the research, revise the informed consent document, inform enrolled subjects, increase monitoring of subjects, etc.); and confirmation that the event has been reported in accordance with section XV.30 of this manual. If the IRB Chairperson disagrees with the action taken by the Principal Investigator or study coordinator, the IRB Chairperson may suspend the study and convene a committee or call a special meeting of the IRB to review the matter.

G. Pursuant to federal regulations and federal guidance, the IRB will advise that the Principal Investigator or study coordinator will report SAEs and UPs to OHRP and the regional office of the Food and Drug Administration as appropriate. The report will include Centra Health, Inc. as the name of the institution conducting the research; title of the research project and/or grant proposal in which the problem occurred; name of the principal investigator on the protocol; number of the research project assigned by the IRB and the number of any applicable federal award(s) (grant, contract, or cooperative agreement) if any; a detailed description of the problem; and 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, etc.).

XVI. NOTIFICATION

Following any vote by the IRB or significant discussion as to protocol pertaining to a particular study, the IRB Chairperson will notify in writing the Principal Investigator and study coordinator of the IRB’s action, including any particular finding(s) or concern(s). Such notice should be provided within five (5) business days following the IRB meeting at which the vote, action or discussion took place.

XVII. CONFIDENTIALITY

It is the responsibility of each Principal Investigator to give written assurance at the time of application to the IRB that subject confidentiality will be protected. Implicit statements or confidentiality protection are not sufficient and some explicit acknowledgements and description of the method by which sensitive human data will be protected are required.

XVIII. COMPENSATION OF SUBJECTS

30 Section XV. of this manual
While it is acceptable to compensate subjects for discomfort or inconvenience resulting from their participation in investigational activities, investigators must not offer undue inducements in recruiting subjects. Compensation may take the form of monetary payments, reduced or waived fees for diagnostic or therapeutic services. In no case should an offer of compensation constitute inducement to take risk, nor should the amount of compensation be based on any degree of risk. Where risk is minimal or very low, and subjects expect no medical benefits to themselves to result from participation in investigational activities, it is reasonable for the investigator to offer compensation which does not exceed in value the equivalent of the subject’s expenses plus a fair wage for the subject’s time, inconvenience and discomfort.

Where subjects may be expected to gain some medical benefits from participating in an investigational activity, or where subjects may undergo more than very low risk, compensation should not exceed the value of actual expenses or losses incurred by subjects as a result of their participation. Investigators should take care when recruiting patients not to take advantage of populations likely to be unduly influenced by the form of compensation offered. If compensation is offered, the investigator must:

A. Explain the nature of compensation and the basis for offering (if compensation is to be pro-rated for subjects completing only part of the study, the basis for pro-rating should be explained).

B. State how subjects to be compensated will be recruited.

C. Include in the consent form a description of the nature of the compensation and, if applicable, the basis for pro-rating compensation for subjects who fail to complete their participation in the investigational activity.

XIX. IRB OBSERVATION

In order to monitor Principal Investigator compliance with IRB policy or federal and/or state regulatory requirements, the IRB reserves the right to appoint one or more of its members or a designated third party to observe any activity under the approved study, particularly pertaining to consent process and/or research. Such observation may be carried out at the discretion of the IRB. Any refusal by a Principal Investigator or study coordinator to an IRB request for observation will be grounds for the imposition of sanctions by the IRB, including suspension and/or termination of the study.
Approvals

Origin Date: Version 1 January 1990
Update: Version 2 October 4, 1990
Reviewed: Version 3 January 2000
Recommendations IRB P&P Committee: 9/25/09, 12/9/09; Approved by Full Board: V. 4 1/13/2010
Recommendations IRB P&P Committee 2/16/11 and 2/21/11; Approved by Full Board: V. 5 2/22/2011
Recommendations IRB P&P Committee 5/25/11; Approved by Full Board: V. 6 June 22, 2011
Recommendation IRB P&P Committee: November 2, 201; Approved by Full Board: V. 7 January 11, 2012
Approved by Full Board: Version 7a December 18, 2012 (no changes)
Recommendation IRB P&P Committee: 10/15/12, 11/02/12, 11/07/12, 1/10/13; Exec Committee 11/27/12, 12/17/12; Approved by Full Board: Version 8 January 15, 2013
Recommendation IRB P&P Committee: 5/2/13; Approved by Full Board: Version 9 June 18, 2013
Recommendations Ad Hoc committee (6.25.13) and IRB P&P Committee (9.06 & 30.13); Approved by Full Board: Version 10 October 15, 2013
Recommendation P&P Committee 12MAR2014 approved by Full Board: Version 11 22APR2014
Recommendations made at the Full Board meeting approved by Full Board: Version 12 20MAY2014
Recommendations Policy Committee (1/30/15; 2/11/15) approved by Full Board: Version 14 25FEB2015
Recommendation Policy Committee (3/23/15) approved by Full Board; Version 14a 21APR2015
Recommendation Policy Committee (3/23/15) approved by Full Board; Version 14b 23JUN2015
P&P Committee meeting 1/6/16, 8/23/16; 9/8/16, 10/19/16, 11/9/16
Recommendation Policy Committee (11/9/16) approved by Full Board; Version 15 15NOV2016
Recommendation Policy Committee (12/19/17) approved by Full Board; Version 16 19DEC2017
P&P Committee meeting 12/11/18; 1/4/19, 1/23/19
Recommendation Policy Committee (2/19/19) approved by Full Board; Version 17 19FEB2019
Edit I. and III. Selection approved by Full Board 05NOV2019
Recommendation Policy Committee (3/2/20) Version 19 approved by IRB Executive Committee 18MAR2020
IRB Organization Information

IORG0001964 - Centra Health (Active)

| Located at: Lynchburg, VIRGINIA |
| Expires: 01/28/2022 |

IRBs for this Organization: 1

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Department of Health and Human Services (DHHS) | Office for Human Research Protections (OHRP) | Accessibility
Institutional Review Board Information

Parent Institution/Organization: IORG0001964 - Centra Health (Active)

Located at: Lynchburg, VIRGINIA
Expires: 01/28/2022

IRB00002475 - Centra Hlth IRB #1 - biomedical (Active)

Located at: Lynchburg, VIRGINIA
Membership Last Updated: 01/28/2019

Assurances Relying Upon this IRB

Total Records: 1 Total Pages: 1 Results per page: 20 Go

Agency Only Access

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**Assurance: Centra Health IRB**

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**Located at:** Lynchburg, VIRGINIA  
**Expires:** 3/11/2025

**Agency Only Access**

**Note:** No Assurance Components Identified.
**Update/Renew an IRB Registration**

Click each of the following tabs to enter required information or to modify previously entered information.

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Add IRB | IRB Info | Chairperson Info | IRB FTE and/or Protocols | IRB Roster

**IRB Roster listing for: Centra Hlth IRB #1 - biomedical**

Notes: Completion of the IRB roster is required if your IRB is designated on an assurance submitted to OHRP [i.e., a Federalwide Assurance(FWA)]; otherwise, it is optional.

**Roster count: 17**

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<td>Gianakos, Dean</td>
<td>M</td>
<td>M.D., FACP</td>
<td>Y</td>
<td>Physician</td>
<td>Y</td>
<td>Chair</td>
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**Voting Member count: 16**

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<tr>
<th>Member #</th>
<th>Voting Member</th>
<th>Sex (M/F)</th>
<th>Earned Degree(s)</th>
<th>Scientist (S) or Non-scientist (N)</th>
<th>Primary Scientific or Nonscientific Specialty</th>
<th>Affiliation with Institution(s) Y/N</th>
<th>Comments (e.g., co-chair, prisoner rep., advocate, alternate member)</th>
<th>Delete</th>
</tr>
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<tbody>
<tr>
<td>9</td>
<td>Lawton, Tom</td>
<td>M</td>
<td>MBA</td>
<td>N</td>
<td>Accounting</td>
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<td>12</td>
<td>Morrison, Ellen</td>
<td>F</td>
<td>BSN, RN, MBA, CPHRM</td>
<td>Y</td>
<td>Nursing/Risk Management</td>
<td>Y</td>
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<td>15</td>
<td>Washburn, Donna</td>
<td>F</td>
<td>DNP, RN, ACNS-BC</td>
<td>Y</td>
<td>Nursing/Professional Clinical Practice</td>
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<td>22</td>
<td>Gillette, Michael A.</td>
<td>M</td>
<td>Ph.D.</td>
<td>N</td>
<td>Ethics</td>
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<td>27</td>
<td>Burgess, Beth</td>
<td>F</td>
<td>n/a</td>
<td>N</td>
<td>Administration</td>
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<td>29</td>
<td>Brunet, Vicky</td>
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<td>DNP, MSN Ed, NNP-BC</td>
<td>Y</td>
<td>Nursing Research</td>
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<td>Trent, Holly B.</td>
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<td>Esq</td>
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<td></td>
<td>Name</td>
<td>Gender</td>
<td>Degree, Certification</td>
<td>Occupation</td>
<td>Training Area</td>
<td>Affiliation</td>
<td>Notes</td>
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<td>Collins, Sean</td>
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<td>Ph.D., CSCS*D</td>
<td>Legal/General Counsel</td>
<td>Exercise Physiology/Education</td>
<td>N</td>
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<td>36</td>
<td>Hill, Frances</td>
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<td>RNC-OB, IBCLC</td>
<td>Legal/General Counsel</td>
<td>Nursing, Pediatrics, Obstetrics</td>
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<td>Delzingaro, Christina</td>
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<td>MBA</td>
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<td>Business</td>
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<td>40</td>
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<td>PharmD, BCPS</td>
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<td>Pharmacy</td>
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<td>41</td>
<td>Miller, Darren</td>
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<td>M.Div., BCC</td>
<td>Legal/General Counsel</td>
<td>Chaplain</td>
<td>Y</td>
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<td>42</td>
<td>Wiggins, Jeff</td>
<td>M</td>
<td>JD, MHA, CHC, CICA</td>
<td>Legal/General Counsel</td>
<td>Corporate Compliance</td>
<td>Y</td>
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<td>43</td>
<td>Lewis, Christopher</td>
<td>M</td>
<td>M.D., MMM, CPE</td>
<td>Legal/General Counsel</td>
<td>Administration, Cardiologist</td>
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<td>44</td>
<td>Bennett, Paul</td>
<td>M</td>
<td>M.D.</td>
<td>Legal/General Counsel</td>
<td>Hospitalist</td>
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<td>46</td>
<td>Follett, Jenny</td>
<td>F</td>
<td>MSN, NP-BC</td>
<td>Legal/General Counsel</td>
<td>Nursing</td>
<td>Y</td>
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</table>

Alternate count: 0

Notes:

1. Members whose training, background, and occupation would incline them to view scientific activities from the standpoint of someone within a behavioral or biomedical research discipline should be considered a scientist, while members whose training, background, and occupation would incline them to view research activities from a standpoint outside of any biomedical or behavioral scientific discipline should be considered a nonscientist. In addition, the IRB must have members with sufficient knowledge of the specific scientific discipline(s) relevant to the research that it reviews.

2. Affiliation: Please indicate whether or not each individual (or a member of that person’s immediate family) is affiliated (other than as an IRB member) with the institution or organization operating the IRB.
   - Yes = The IRB member is affiliated with the institution or organization operating the IRB.
   - No = The individual is not affiliated with the institution or organization operating the IRB.

3. Alternate Members: An alternate member(s) may be designated, as needed, for a regular voting member(s). An alternate member may vote only when the regular voting member is not voting.

When an institution or organization registers two or more IRBs, all alternate members for all IRBs may be listed on the roster of one IRB, or they may be listed separately with each IRB roster. A primary member of any IRB registered under the same IORG number may serve as an alternate for any comparably qualified member on any other IRB of that institution or organization. Primary members on registered IRBs serving as alternate members do not need to be listed as an alternate on any roster. Each alternate IRB member who replaces a primary member at any given meeting should have experience, expertise, background, professional competence, and knowledge equivalent to that of the primary IRB member whom the alternate will replace. Whenever an alternate member substitutes for a primary member of the IRB, the combined requirements of § 46.107(a) and 46.108(b) shall remain satisfied. Whenever this occurs, the minutes of the IRB meeting should indicate clearly that the alternate IRB member has replaced the designated primary IRB member, and include the identity of the replaced primary and the alternate members. If multiple alternate members serve at an IRB meeting, the pairing of primary and alternate members should be indicated.

Public burden for this collection of information is estimated to average one hour for an initial IRB registration, and thirty minutes for updating or renewing the registration of a previously registered IRB. An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number. Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden to: OS Reports Clearance Officer, Room 537H, 200 Independence Avenue, SW., Washington, DC 20201. Do not return the completed form to this address.
An IRB Member must disclose all potential conflict of interests to the IRB office. If the IRB determines that a conflict exists that could influence research or jeopardize the well-being of research subjects, or influence the IRB member’s review of a research project, the IRB may require additional information about the conflict, may require the conflict to be resolved before the IRB member votes on the approval of a research protocol, or may require that due to the conflict, the IRB member should be recused from evaluating protocols that involve the conflict. You should consider your current business and personal relationships within the preceding 12 months, including your affiliations with Centra Health and its subsidiaries, in completing this Conflict of Interest Disclosure Form.

Definitions:

**Conflict of Interest**: means any situation or circumstance in which an IRB Member or a Related Party has a financial, personal, or other interest (including, but not limited to, an Individual Interest, Financial Interest, or Institutional Interest) which conflicts with, compromises, or has the appearance of conflicting with or compromising the individual’s independent judgment and objectively rendering the member incapable of making an unbiased and objective decision regarding the research.

**Financial Interest**: Anything of monetary value received from a financially interested company, including but not limited to: director’s fees; consulting fees; honoraria; gifts; other emoluments or “in kind” compensation such as travel and entertainment (including those from a third party if the original source is a financially interested company), for any services not directly related to the reasonable costs of conducting the research as specified in the research agreement; equity interest (e.g., stocks, stock options, convertible notes, other ownership interests); and intellectual property rights (e.g., license fees, current and future royalties from patents and copyrights).

The term “Financial Interest” does not include:

1. Salary or other remuneration received from [Hospital];
2. Holdings in mutual funds;
iii. De minimus gifts whose aggregate value does not exceed $100 per annum; or reasonable business expenses, including travel and meals provided in the regular course of business.

**Institutional Interest:** means that the individual is affiliated with an institution and that the interests of the institution either affect or appear to affect institutional processes such as the conduct, review and oversight of human research; for example, ownership in a company that holds a patent to a new drug or device.

**IRB Conflict of Interest Committee:** means an Ad Hoc Committee established by the IRB Chairperson to review all IRB members’ conflicts of interest disclosure forms and manage potential conflicts.

**Related Party:** IRB member’s spouse, domestic partner, or dependent children, siblings, parents, or equivalents by marriage, or other individuals residing in the IRB member’s household.

__ Yes __ No Do you or any Related Party have a “Financial Interest” or “Institutional Interest” in either a public or private company whose drug, procedure, technique, device or product is used or tested in human subject research at Centra Health or with any company making a competing product?

Explain: _________________________________________________________

__________________________________________________________________
__________________________________________________________________

__ Yes __ No Have you or any Related Party received support or gifts (whether in dollars or in kind) from a pharmaceutical manufacturing, research, or distribution company which could be affected by conduct or outcome of a research project at Centra Health?

Explain: _________________________________________________________

__________________________________________________________________
__________________________________________________________________

__ Yes __ No Have you or any Related Party (i) served on a board of directors or advisory board; (ii) held an executive position; (iii) served as a consultant to; (iv) served on the speaker bureau; or (v) owned any stock, stock options or other forms of ownership in a company that could be affected by the conduct or outcome of research at Centra Health?
Explain: _________________________________________________________
_________________________________________________________________
_________________________________________________________________

__ Yes__ No Are you affiliated with Centra Health? Affiliation includes Related
Party who is affiliated with Centra Health.
Explain: _________________________________________________________
_________________________________________________________________
_________________________________________________________________

__ Yes__ No Have you (i) been involved in the design, conduct or reporting of clinical
research trials at Centra Health; (ii) participated in funded or unfunded
research at Centra Health; or (iii) participated in technology, process, or
product development related to human subject research activities in which
the value of your compensation could be affected by the study outcome?
Explain: _________________________________________________________
_________________________________________________________________
_________________________________________________________________

__ Yes__ No Do you have any other interest that may appear to conflict with the
protection of human research subjects or which may involve a potential or
actual research protocol at Centra Health?
Explain: _________________________________________________________
_________________________________________________________________
_________________________________________________________________

Your signature below is your representation that the information provided
above and on attached sheets is, to the best of your knowledge, accurate. You must
advise the Chairman of the IRB Board promptly of any subsequent circumstances which
arise and which may come within scope or spirit of the Conflict of Interest Disclosure
Statement.

____________________________________________ __________________________
Signature         Date

Typing my name on the line above constitutes an electronic signature.
The purpose of this application is to seek initial IRB approval for a research study. The Principal Investigator is the person who will personally conduct or supervise this research study.

There are three levels of IRB Review [full board, expedited (only applies after initial approval), and exempt refer to FDA 45CFR 46 101(b)], determined by the nature of the project, level of potential risk to human subjects, and the subject population. The type of review applicable to a particular study is determined by the IRB.

Please read the following to answer the question below:

Do the HHS regulations for the protection of human subjects in research (45 CFR part 46) apply to quality improvement activities conducted by one or more institutions whose purposes are limited to: (a) implementing a practice to improve the quality of patient care, and (b) collecting patient or provider data regarding the implementation of the practice for clinical, practical, or administrative purposes?

No, such activities do not satisfy the definition of "research" under 45 CFR 46.102(d), which is "...a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge..." Therefore, the HHS regulations for the protection of human subjects do not apply to such quality improvement activities, and there is no requirement under these regulations for such activities to undergo review by an IRB, or for these activities to be conducted with provider or patient informed consent.

Having read the above, is this research? If yes, continue to fill out the form.

Submission Instructions
This form is in Word format.
- Click into the highlighted area (      ) requesting an answer and type your answers into the form.
- Save the form.
- Send the application and all other pertinent documentation ( ie protocol, informed consent, etc.) electronically as a pdf via email to irb@centrahealth.com.

What parts of this application should you submit?
Answer all questions, or mark “not applicable,” when appropriate. Do not alter wording or delete questions from this form.
- For all studies, submit Part A, which consists of these sections:
  - Part A.1. Contact Information, Agreements, and Signatures
  - Part A.2. Summary Checklist
  - Part A.3. Conflict of Interest Questions and Certification
  - Part A.4. Questions Common to All Studies
  - Part A.5. The Consent Process and Consent Documentation (including Waivers)
- For studies that involve direct interaction with human subjects (any contact with subjects including questionnaires, interviews, focus groups, observation, treatment interventions, etc), submit:
  - Part B. Questions for Studies that Involve Direct Interaction with Human Subjects
- For studies that use existing data, records or human biological specimens, including for use in identifying potential subjects, submit:
  - Part C. Questions for Studies using Existing Data, Records or Human Biological Specimens

Note: You should submit Parts B or C only as applicable. If the study involves both direct interaction and use of existing materials, use both Parts B and C in addition to Part A.

Address for all Applications and Other Correspondence
irb@centrahealth.com electronically
CENTRA HEALTH - Institutional Review Board
APPLICATION FOR IRB APPROVAL OF HUMAN SUBJECTS RESEARCH
Version 14 17MAR2020

Part A.1. Contact Information, Agreements, and Signatures

Date:

CHIRB#: (Will be assigned upon receipt)

Title of Study:

Name and degrees of Principal Investigator:
Department: Mailing address:

Phone #: Fax #: Email Address:

Center, institute, or department in which research is based if other than department(s) listed above:

Name of Project Manager or Study Coordinator (if any):
Department: Mailing address/CB #:
Phone #: Fax #: Email Address:

List all other project personnel including co-investigators, and anyone else who has contact with subjects or identifiable data from subjects. Include name, location (local site or specific outside location), role and email address for each person who should receive electronic copies of IRB correspondence to PI.

Name of funding source or sponsor (please do not abbreviate):
__ not funded __ Federal __ State __ industry __ foundation __ other (specify):

Name of IRB of Record: Centra Health IRB or Other: ______________________

For industry sponsored research (if applicable):

Sponsor’s master protocol version #: Version date:
Investigator Brochure version #: Version date:

IND (Investigational New Drug) #:
IDE (Investigational Device Exemption) #:

For FDA Required Monitoring for:
HUD (Humanitarian Use Device) #: HDE (Humanitarian Device Exemption) #:
Sponsors determination of risk: Significant Risk Study [ ] Non-Significant Risk Study [ ]
Any other details you need documented on IRB approval:
Checklist of Items to Include with Your Submission

Include the following items with your submission, where applicable.

- Check the relevant items below and either send electronically (by email to irb@centrahealth.com) or include one copy of all checked items 1-10 in the order listed.

Applications will be returned if these instructions are not followed.

<table>
<thead>
<tr>
<th>Check</th>
<th>Item</th>
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<tbody>
<tr>
<td>☐</td>
<td>1. This application and all other applicable documents checked below electronically (by email to <a href="mailto:irb@centrahealth.com">irb@centrahealth.com</a>).</td>
</tr>
<tr>
<td>☐</td>
<td>2. Consent and assent forms (include DHHS-approved sample, when one exists), fact or information sheets, phone and verbal consent scripts. Include Fact Sheet or Script as applicable for any research where consent is waiver. (See A.5.2.a and A.5.3)</td>
</tr>
<tr>
<td>☐</td>
<td>3. HIPAA authorization (Form 7) and/or PHI: Waiver of Authorization (Form 5) as needed.</td>
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<tr>
<td>☐</td>
<td>4. All recruitment materials including final copies of printed advertisements, audio/video taped advertisements, scripts, flyers, letters, and emails.</td>
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<tr>
<td>☐</td>
<td>5. Questionnaires, focus group guides, scripts used to guide phone or in-person interviews, etc. and documentation of Human Resource approval for distribution of questionnaires to Centra employees.</td>
</tr>
<tr>
<td>☐</td>
<td>6. Documentation of approvals from any other stakeholders responsible for Centra location/department/employees where research will take place.</td>
</tr>
<tr>
<td>☐</td>
<td>7. Protocol, grant application or proposal supporting this submission, if any (e.g., extramural grant application to NIH or foundation, industry protocol, student proposal). This must be submitted if an external funding source or sponsor is checked on the previous page.</td>
</tr>
<tr>
<td>☐</td>
<td>8. Data use agreements (may be required for use of existing data from third parties).</td>
</tr>
<tr>
<td>☐</td>
<td>9. For drug studies, Investigator Brochure if one exists. If none, include package insert for previously approved uses.</td>
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<tr>
<td>☐</td>
<td>10. IRB or other committee/board approvals from outside institutions as applicable.</td>
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Principal Investigator: I will personally conduct or supervise this research study. I will ensure that this study is performed in compliance with all applicable laws, regulations and Centra Health’s policies regarding human subjects research. I will obtain IRB approval before making any changes or additions to the project. I will notify the IRB of any other changes in the information provided in this application. I will provide progress reports to the IRB at least annually, or as requested. I will report within five (5) business days to the IRB all unanticipated problems or serious adverse events involving risk to human subjects. I will follow the IRB approved consent process for all subjects. I will ensure that all collaborators, students and employees assisting in this research study are informed about these obligations. All information given in this form is accurate and complete.

Signature of Principal Investigator

Typing my name on the line above constitutes an electronic signature.

Date
### Part A.2. Summary Checklist

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<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
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<tr>
<td>A.2.1 Is the study to be conducted at a Centra facility?</td>
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<tr>
<td>A.2.2 Does the study utilize existing data, research records, patient records, and/or human biological specimens?</td>
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<tr>
<td>A.2.3 Does the study utilize surveys, questionnaires, interviews, or focus groups with subjects?</td>
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<tr>
<td>A.2.4 Does the study require videotaping, audiotaping, filming of subjects, or analysis of existing tapes?</td>
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<tr>
<td>A.2.5.1 Do you have specific plans to enroll subjects from these vulnerable or select populations:</td>
<td></td>
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</tr>
<tr>
<td>a. Centra Health’s employees? If this is a survey of Centra employees, it is mandatory the study has been approved by Human Resources? If yes, please include documentation of approval.</td>
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<tr>
<td>b. Non-English-speaking?</td>
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<td></td>
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<tr>
<td>c. Decisionally impaired?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>d. Centra patients?</td>
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<tr>
<td>e. Prisoners, others involuntarily detained or incarcerated, or parolees?</td>
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<tr>
<td>f. Pregnant women?</td>
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<tr>
<td>g. Minors (less than 18 years)? If yes, give age range: to years</td>
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<tr>
<td>h. Handicapped?</td>
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<tr>
<td>A.2.5.2 If b., c., e., f., or g. are checked yes, are there additional safeguards in place and what are they?</td>
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<tr>
<td>A.2.6 a. Are sites outside Centra Health engaged in the research?</td>
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<td></td>
</tr>
<tr>
<td>b. Is Centra Health the sponsor or lead coordinating center multi-site study?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes, include the Addendum for Multi-site Studies.</td>
<td></td>
<td></td>
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<tr>
<td>If yes, will any of these sites be outside the United States?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If yes, is there a local ethics review committee agency with jurisdiction? (provide contact information)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>c. If the study is eligible for IRB or equivalent approval by the Institution of higher education, IRB approval from said institution must be obtained and submitted to the Centra IRB before study can be initiated. A study may be approved pending gaining approval from the educational IRB.</td>
<td></td>
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</tr>
<tr>
<td>A.2.7. Will this study use a data and safety monitoring board or committee?</td>
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<td></td>
</tr>
<tr>
<td>If yes: Specify:</td>
<td></td>
<td></td>
</tr>
<tr>
<td>a. Are you collecting sensitive information such as sexual behavior, HIV status, recreational drug use, illegal behaviors, child/physical abuse, immigration status, etc?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>b. Do you plan to obtain a federal Certificate of Confidentiality for this study?</td>
<td></td>
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</tr>
<tr>
<td>c. Is this research classified (e.g., requires security clearance)?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A.2.9 Does the study utilize:</td>
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</tr>
<tr>
<td>a. Investigational drugs? (provide IND # )</td>
<td></td>
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</tr>
<tr>
<td>b. Approved drugs for “non-FDA-approved” conditions?</td>
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<tr>
<td>c. Are the investigational drugs/devices stored securely under the conditions recommended by the protocol/manufacturer?</td>
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<tr>
<td>A.2.10. Does the study utilize placebo(s)?</td>
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<tr>
<td>A.2.11 Investigational devices, instruments, machines, software? (provide IDE # )</td>
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<tr>
<td>If yes, is it categorized as Significant Risk or Nonsignificant Risk? (Circle one)</td>
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<tr>
<td>Devices FDA requires monitoring: (provide HUD# )</td>
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<tr>
<td>(provide HDE# )</td>
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<tr>
<td>A.2.12 Does the study utilize fetal tissue?</td>
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</table>
A.2.13. Will there be genetic studies on subjects’ specimens?

A.2.14. Will there be storage of subjects’ specimens for future research?  
*If yes, attach a sample of Consent for Stored Samples.*

A.2.15. Does the study include diagnostic or therapeutic ionizing radiation, or radioactive isotopes, which subjects would not receive if not enrolled in the investigation?

- a. If yes, does the dose that research subjects will receive from undergoing a procedures or series of procedures exceed a total effective cumulative dose of 100 mSv (0.1Sv, 10rem, 10,000 mrem)?  
  *If yes, the study must be referred to the Radiation Safety and Medical Isotopes Committee by the Chairman of the IRB and the RSC must make a recommendation to the IRB before the IRB can review the study.*

- b. Will the patient be subject to deterministic effects from radiation exposure such as skin erythema, epilation, desquamation, or cataracts as a result of receiving doses above 2 Gy (200 rad)?  
  *If yes, the study must be referred to the Radiation Safety and Medical Isotopes Committee by the Chairman of the IRB and the RSC must make a recommendation to the IRB before the IRB can review the study.*

  Note: a dose estimation tool can be found at [http://www.doseinfo-radar.com/RADARDoseRiskCalc.html](http://www.doseinfo-radar.com/RADARDoseRiskCalc.html)

A.2.16. Will there be recombinant DNA or gene transfer to human subjects?

A.2.17. Will gadolinium be administered as a contrast agent?

A.2.18. Will subjects’ Social Security Number (SSN) be collected for:  
- a. processing payments greater than $200 per year, to support IRS reporting (see also B.6)?  
- b. processing payments of any amount through Centra Health Accounts Payable?  
- c. use as a unique identifier for study tracking purposes for national registry or database?

A.2.19 Has the level of risk to the subject been described in the application?

A.2.20 What is the level of risk to the subject? Circle one:

- a. None  
- b. Minimal risk  
- c. Greater than minimal risk but potential direct benefit  
- d. Greater than minimal risk and no direct benefit, but has potential to yield generalized knowledge about the subject’s disorder or condition.

A.2.21 If the risk is greater than minimal, are the risks reasonable in relation to the potential benefit in the investigator’s opinion?

A.2.22 Are the potential benefits to subjects adequately described in the application?

A.2.23 Are the study groups clearly described in the protocol?

A.2.24 Are the objectives and outcome measures consistent with the rationale?

A.2.25 Are experimental procedures distinguished from the standard of care or treatment?

A.2.26 Are provisions in place to maintain the confidentiality of the data and subject information?

A.2.27 Are the costs to be borne by subjects accurately described?

A.2.28 Have you included in your protocol who will bear financial responsibility for any complications that may occur as a result of participation?

A.2.29 Are the data monitoring provisions adequate for subject safety?

A.2.30 Have you included in your protocol who will bear financial responsibility for any
<table>
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<tr>
<th>Question</th>
<th>Answer</th>
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<tr>
<td>A.2.31 Is Informed Consent required as part of your study? For research where there is interaction with live subjects, a consent process is normally required. Please include a copy of the consent. On the rare occasion that verbal consent is used, please include a copy of the script.</td>
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<tr>
<td>A.2.32 Does the consent contain the notice provisions dealing with the description of the trial including a reference to <a href="http://www.Clinical">http://www.Clinical</a> Trials.gov? This is required for all drug and device trials regulated by the FDA. Please indicate page number on ICF:</td>
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<tr>
<td>A.2.33 Do you have the resources available to properly administer the consent process?</td>
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<td>A.2.34 Is there any information that is not contained in the study protocol or information that the IRB should know about? If yes, attach full explanation.</td>
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<tr>
<td>A.2.35 Have you included a Curriculum Vitae (CV)/Resume of the Principal Investigator.</td>
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<tr>
<td>A.2.36 Does this study involve surveying Centra employees? If yes, please obtain Human Resource approval prior to submission &amp; include in your application. The contact for the HR department is VP HR at 434-200-5342.</td>
<td></td>
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<tr>
<td>A.2.37. Has the study been reviewed by a committee or expert such as a statistician to ensure ideal statistical methods are being used? Review should include study design, sample size, and planned statistical evaluation of the study.</td>
<td></td>
</tr>
<tr>
<td>A.2.38 If any existing texts/tools/questionnaires/instruments/and other methods of data collection are used in the study, has permission for use been obtained (Please note: if there is potential for publication, this will also be required by the publisher.)</td>
<td></td>
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<tr>
<td>- Is the above in A.2.38 been validated? (Using a non-validated instrument could potentially cause unnecessary anxiety or risk to the participant.)</td>
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</table>
Part A.3. Centra Institutional Review Board
Conflict of Interest Questions and Certification

The following questions apply to all IRB Principal Investigators and/or Study Doctors and Study Coordinators engaged in the design, conduct, or reporting results of this project and/or Related Party.

Definitions:

**Related Party** is the Principal Investigator’s and/or Study Doctor and Study Coordinator’s spouse, domestic partner, or dependent children, siblings, parents or equivalents by marriage, or other individuals residing in the PI/Study Coordinator’s household.

**Financial Interest:** Anything of monetary value received from a financially interested company, including but not limited to: director’s fees; consulting fees; honoraria; gifts; other emoluments or “in kind” compensation such as travel and entertainment (including those from a third party if the original source is a financially interested company), for any services not directly related to the reasonable costs of conducting the research as specified in the research agreement; equity interest (e.g., stocks, stock options, convertible notes, other ownership interests); and intellectual property rights (e.g., license fees, current and future royalties from patents and copyrights).

The term “Financial Interest” does not include:

i. Salary or other remuneration received from [Hospital];

ii. Holdings in mutual funds;

iii. De minimus gifts whose aggregate value does not exceed $100 per annum; or reasonable business expenses, including travel and meals provided in the regular course of business.

**Conflict of Interest:** means any situation or circumstance in which an IRB Member or a Related Party has a financial, personal, or other interest (including, but not limited to, an Individual Interest, Financial Interest, or Institutional Interest) which conflicts with, compromises, or has the appearance of conflicting with or compromising the individual’s independent judgment and objectively rendering the member incapable of making an unbiased and objective decision regarding the research.

A.3.1. Currently or during the term of this research study, does any member of the research team or a Related Party have or expect to have:

(a) A personal financial interest in or personal financial relationship (including gifts of cash or in-kind) with the sponsor of this study?

   Explain: _________________________________________________________

   __ yes ___ no

(b) A personal financial interest in or personal financial relationship (including gifts of cash or in-kind) with an entity that owns or has the right to commercialize a product, process or technology studied in this project?

   Explain: _________________________________________________________

   __ yes ___ no

(c) A personal financial interest in or personal financial relationship (including gifts of cash or in-kind) with an entity engaged in the performance of this project as a subcontractor, sub-recipient or vendor?

   Explain: _________________________________________________________

   __ yes ___ no

(d) A board membership of any kind or an executive position (paid or unpaid) with the
<table>
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<tr>
<th>Question</th>
<th>Yes</th>
<th>No</th>
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<tr>
<td>A.3.2. Has Centra Health or has Centra Health-related foundation received a cash or in-kind gift from the sponsor of this study for the use or benefit of any member of the research team?</td>
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<td>Explain:</td>
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<tr>
<td>A.3.3. Has Centra Health or has a Centra Health-related foundation received a cash or in-kind gift for the use or benefit of any member of the research team from an entity that owns or has the right to commercialize a product, process or technology studied in this project?</td>
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<td>Explain:</td>
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**If the answer to ANY of the questions above is yes,** list name(s) of all research team members for whom any answer to the questions above is yes:

______________________________

**Certification by Principal Investigator/Study Doctor/Study Coordinator.** By submitting this IRB application, I (the PI/Study Doctor/Study Coordinator) certify that the information provided above is true and accurate regarding my own circumstances, that I have inquired of every Centra Health employee who will be engaged in the design, conduct or reporting of results of this project as to the questions set out above, and that I have instructed any such person who has answered “yes” to any of these questions to complete and submit for approval a Conflict of Interest Evaluation Form. I understand that as Principal Investigator I am obligated to ensure that any potential Conflicts of Interest that exist in relation to my study are reported as required by IRB policy.

Signature of Principal Investigator

Typing my name on the line above constitutes an electronic signature.

Signature of Study Coordinator

Typing my name on the line above constitutes an electronic signature.
Part A.4. Questions Common to All Studies

For all questions, if the study involves only secondary data analysis, focus on your proposed design, methods and procedures, and not those of the original study that produced the data you plan to use.

Complete answers must be provided. While you may reference other documents with supporting information, do not respond solely by stating “see attached.”

A.4.1. **Brief Summary.** Provide a brief non-technical description of the study, which will be used in IRB documentation as a description of the study. Typical summaries are 50-100 words. Please reply to each item below, retaining the subheading labels already in place, so that reviewers can readily identify the content.

**Purpose:**
What is the expected duration of the research?

**Participants:**

**Procedures (methods):**

A.4.2. **Purpose and Rationale.** Provide a summary of the background information, state the research question(s), and tell why the study is needed. If a complete rationale and literature review are in an accompanying grant application or other type of proposal, only provide a brief summary here. If there is no proposal, provide a more extensive rationale and literature review, including references.

A.4.3. **Subjects.** You should describe the subject population even if your study does not involve direct interaction (e.g., existing records). Specify number, gender, ethnicity, race, and age. Specify whether subjects are healthy volunteers or patients. If patients, specify any relevant disease or condition and indicate how potential subjects will be identified. Researchers are reminded that additional approvals may be needed from relevant “gatekeepers” to access subjects (e.g., school principals, facility directors, hospital or healthcare system administrators).

A.4.4. **Inclusion/exclusion criteria.** List required characteristics of potential subjects, and those that preclude enrollment or involvement of subjects or their data. Justify exclusion of any group, especially by criteria based on gender, ethnicity, race, or age. If pregnant women are excluded, or if women who become pregnant are withdrawn, specific justification must be provided.

A.4.5. **Full description of the study design, methods and procedures.** Describe the research study. Discuss the study design; study procedures; sequential description of what subjects will be asked to do; assignment of subjects to various arms of the study if applicable; doses; frequency and route of administration of medication and other medical treatment if applicable; how data are to be collected (questionnaire, interview, focus group or specific procedure such as physical examination, venipuncture, etc.). Include information on who will collect data, who will conduct procedures or measurements. Indicate the number and duration of contacts with each subject; outcome measurements; and follow-up procedures. If the study involves medical treatment, distinguish standard care procedures from those that are research. If the study is a clinical trial involving patients as subjects and use of placebo control is involved, provide justification for the use of placebo controls.

A.4.6. **Benefits to subjects and/or society.** Describe any potential for direct benefit to individual subjects, as well as the benefit to society based on scientific knowledge to be gained; these should be
clearly distinguished. Consider the nature, magnitude, and likelihood of any direct benefit to subjects. If there is no direct benefit to the individual subject, say so here and in the consent form (if there is a consent form). Do not list monetary payment or other compensation as a benefit.

A.4.7. **Full description of risks and measures to minimize risks.** Include risk of psychosocial harm (e.g., emotional distress, embarrassment, breach of confidentiality), economic harm (e.g., loss of employment or insurability, loss of professional standing or reputation, loss of standing within the community) and legal jeopardy (e.g., disclosure of illegal activity or negligence), as well as known side effects of study medication, if applicable, and risk of pain and physical injury. Describe what will be done to minimize these risks. Describe procedures for follow-up, when necessary, such as when subjects are found to be in need of medical or psychological referral. If there is no direct interaction with subjects, and risk is limited to breach of confidentiality (e.g., for existing data), state this.

A.4.8. **Data monitoring and analysis.** Tell how the qualitative and/or quantitative data will be analyzed. Explain how the sample size is sufficient to achieve the study aims. This might include a formal power calculation or explanation of why a small sample is sufficient (e.g., qualitative research, pilot studies). Describe the provisions for monitoring the data to ensure the safety of participants. These plans could range from the investigator monitoring subject data for any safety concerns to a sponsor-based DSMB, depending on the study.

A.4.9. **Will you collect or receive any of the following identifiers?** Does not apply to consent forms.  
  __ No  __ Yes  If yes, check all that apply:

  a. __ Names  
  b. __ Telephone numbers  
  c. __ Any elements of dates (other than year) for dates directly related to an individual, including birth date, admission date, discharge date, date of death. For ages over 89: all elements of dates (including year) indicative of such age, except that such ages and elements may be aggregated into a single category of age 90 and older  
  d. __ Any geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code and their equivalent geocodes, except for the initial three digits of a zip code  
  e. __ Fax numbers  
  f. __ Electronic mail addresses  
  g. __ Social security numbers  
  h. __ Medical record numbers  
  i. __ Health plan beneficiary numbers  
  j. __ Account numbers  
  k. __ Certificate/license numbers  
  l. __ Vehicle identifiers and serial numbers (VIN), including license plate numbers  
  m. __ Device identifiers and serial numbers (e.g., implanted medical device)  
  n. __ Web universal resource locators (URLs)  
  o. __ Internet protocol (IP) address numbers  
  p. __ Biometric identifiers, including finger and voice prints  
  q. __ Full face photographic images and any comparable images  
  r. __ Any other unique identifying number, code, or characteristic, other than dummy identifiers that are not derived from actual identifiers and for which the re-identification key is maintained by the health care provider and not disclosed to the researcher

A.4.10. **Identifiers in research data.** Are the identifiers in A.4.9 above linked or maintained with the research data?
  __ yes  __ no

A.4.11. **Confidentiality of the data.** Describe procedures for maintaining confidentiality of the data you will collect or will receive. Describe how you will protect the data from access by those not authorized. How will data be transmitted among research personnel? Where relevant, discuss the potential for deductive disclosure (i.e., directly identifying subjects from a combination of indirect IDs).
A.4.12. **Data sharing.** With whom will *identifiable* (contains any of the 18 identifiers listed in question A.4.9 above) data be shared outside the immediate research team? For each, explain confidentiality measures. Include data use agreements, if any.

- No one
- Coordinating Center:
- Statisticians:
- Consultants:
- Other researchers:
- Registries:
- Sponsors:
- External labs for additional testing:
- Journals:
- Publicly available dataset:
- Other:

A.4.13. **Data security for storage and transmission.** Please check all that apply.

*For electronic data stored on a desk top computer:*
- Secure network
- Password access
- Data encryption
- Password protected file(s)
- Other comparable safeguard (describe):

*For portable computing devices/external storage devices (e.g. laptop computer, hand held devices, CDs, memory sticks):*
- Power-on password
- Automatic log-off
- Data encryption
- Password protected file(s)
- Other comparable safeguard (describe):

*For hardcopy data (including human biological specimens, CDs, tapes, etc.):*
- Data de-identified by research team (stripped of the 18 identifiers listed in question A.4.9 above)
- Locked suite or office
- Locked cabinet
- Data coded by research team with a master list secured and kept separately
- Other (describe):

A.4.14. **Post-study disposition of identifiable data or human biological materials.** Describe your plans for disposition of data or human biological specimens that are identifiable in any way (directly or via indirect codes) once the study has ended. Describe your plan to destroy identifiers, if you will do so.
Part A.5. The Consent Process and Consent Documentation (including Waivers)

The standard consent process is for all subjects to sign a document containing all the elements of informed consent, as specified in the federal regulations. Some or all of the elements of consent, including signatures, may be altered or waived under certain circumstances.

- If you will obtain consent in any manner, complete section A.5.1.
- If you are obtaining consent, but requesting a waiver of the requirement for a signed consent document, complete section A.5.2.
- If you are requesting a waiver of any or all of the elements of consent, complete section A.5.3.
- If you need to access Protected Health Information (PHI) to identify potential subjects who will then be contacted, you will need a waiver of HIPAA authorization. This is addressed in section B.2.

You may need to complete more than one section. For example, if you are conducting a phone survey with verbal consent, complete sections A.5.1, A.5.2, and possibly A.5.3.

### A.5.1. Describe the process of obtaining informed consent from subjects.

Describe who will be obtaining consent (or permission) and from whom. Include discussion, as relevant, any waiting period between the initial consent discussion and obtaining consent, and steps that will be taken to minimize coercion or undue influence. If children will be enrolled as subjects, describe the provisions for obtaining parental permission and assent of the child. If decisionally impaired adults are to be enrolled, describe the provision for obtaining surrogate consent from a legally authorized representative (LAR). If non-English speaking people will be enrolled, explain how consent in the native language will be obtained. Address both written translation of the consent and the availability of oral interpretation. It is expected that the information in the consent document(s) will be communicated to participants or their LAR. After you have completed this part A.5.1, if you are not requesting a waiver of any type, you are done with Part A.5.; proceed to Part B. For additional information on informed consent, including a checklist of all required elements, please visit:


### A.5.2. Justification for a waiver of written (i.e., signed) consent.

The default is for subjects to sign a written document that contains all the elements of informed consent. Under limited circumstances, the requirement for a signed consent form may be waived by the IRB if either of the following is true. **Choose only one:**

- a. 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 (e.g., study topic is sensitive so that public knowledge of participation could be damaging). *Participants should be asked whether they want documentation linking them with the research and the participants’ wishes will govern whether they sign the form.* Note: This justification cannot be used in FDA-regulated research.

  \[\text{__ yes __ no}\]

  **Explain.**

- b. 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 (e.g., phone survey).

  \[\text{__ yes __ no}\]

  **Explain.**
If you checked “yes” to either (and you are not requesting a waiver in section A.5.3) consent must be obtained orally, by delivering a fact sheet, through an online consent form, or be incorporated into the survey itself. Include a copy of the consent script, fact sheet, online consent form, or incorporated document.

→ If you have justified a waiver of written (signed) consent (A.5.2), you should complete A.5.3 only if your consent process will not include all the other elements of consent

A.5.3. Justification for a full or partial waiver of consent. The default is for subjects to give informed consent. A waiver might be requested for research involving only existing data or human biological specimens (see also Part C). More rarely, it might be requested when the research design requires withholding some study details at the outset (e.g., behavioral research involving deception). In limited circumstances, parental permission may be waived. This section should also be completed for a waiver of HIPAA authorization if research involves Protected Health Information (PHI) subject to HIPAA regulation, such as patient records.

__ Requesting waiver of some elements
__ Requesting waiver of consent entirely

If you check either of the boxes above, answer items a-f. To justify a full waiver of the requirement for informed consent, you must be able to answer “yes” (or “not applicable” for question c) to items a-f. Insert brief explanations that support your answers.

a. Will the research involve no greater than minimal risk to subjects or to their privacy? __ yes __ no
Explain.

b. Is it true that the waiver will not adversely affect the rights and welfare of subjects? (Consider the right of privacy and possible risk of breach of confidentiality in light of the information you wish to gather.) __ yes __ no
Explain.

c. When applicable to your study, do you have plans to provide subjects with pertinent information after their participation is over? (e.g., Will you provide details withheld during consent, or tell subjects if you found information with direct clinical relevance? This may be an uncommon scenario.) __ yes __ not applicable
Explain.

d. Would the research be impracticable without the waiver? (If you checked “yes,” explain how the requirement to obtain consent would make the research impracticable, e.g., are most of the subjects lost to follow-up or deceased?). __ yes __ no
Explain.

e. Is the risk to privacy reasonable in relation to benefits to be gained or the importance of the knowledge to be gained? __ yes __ no
Explain.

If you are accessing patient records for this research, you must also be able to answer “yes” to item f to justify a waiver of HIPAA authorization from the subjects.

f. Would the research be impracticable if you could not record (or use) Protected Health Information (PHI)? (If you checked “yes,” explain how not recording or using PHI would make the research impracticable). __ yes __ no
Explain.
Part B. Questions for Studies that Involve Direct Interaction with Human Subjects

→ If this does not apply to your study, do not submit this section.

B.1. Methods of recruiting. Describe how and where subjects will be identified and recruited. Indicate who will do the recruiting, and tell how subjects will be contacted. Describe efforts to ensure equal access to participation among women and minorities. Describe how you will protect the privacy of potential subjects during recruitment. For prospective subjects whose status (e.g., as patient or client), condition, or contact information is not publicly available (e.g., from a phone book or public web site), the initial contact should be made with legitimate knowledge of the subjects’ circumstances. Ideally, the individual with such knowledge should seek prospective subjects’ permission to release names to the PI for recruitment. Alternatively, the knowledgeable individual could provide information about the study, including contact information for the investigator, so that interested prospective subjects can contact the investigator. Provide the IRB with a copy of any document or script that will be used to obtain the patients’ permission for release of names or to introduce the study. Check with the IRB for further guidance.

B.2. Protected Health Information (PHI). If you need to access Protected Health Information (PHI) to identify potential subjects who will then be contacted, you will need a waiver of HIPAA authorization. If this applies to your study, please complete Form 5.

B.3. Duration of entire study and duration of an individual subject’s participation, including follow-up evaluation if applicable. Include the number of required contacts and approximate duration of each contact.

B.4. Where will the subjects be studied? Describe locations where subjects will be studied, both on and off the Centra Health campus

B.5. Privacy. Describe procedures that will ensure privacy of the subjects in this study. Examples include the setting for interviews, phone conversations, or physical examinations; communication methods or mailed materials (e.g., mailings should not indicate disease status or focus of study on the envelope).

B.7. Costs to be borne by subjects. Include childcare, travel, parking, clinic fees, diagnostic and laboratory studies, drugs, devices, all professional fees, etc. If there are no costs to subjects other than their time to participate, indicate this.

Part C. Questions for Studies using Existing Data, Records or Human Biological Specimens

→ This section may apply even if records are used to identify potential subjects.

→ If your study does not use existing data, records or specimens for any purpose, do not submit this section.

C.1. What records, data or human biological specimens will you be using? (check all that apply):

__ Data already collected for another research study
If applicant was involved in the original collection, please explain role:

__ Data already collected for administrative purposes (e.g., Medicare data, hospital discharge data)
__ Medical records
__ Electronic information from clinical database (custodian may also require form)
__ Patient specimens (tissues, blood, serum, surgical discards, etc.)
__ Other (specify):

C.2. Protected Health Information (PHI). If any of the above checked items constitute Protected Health Information, you need a HIPAA Authorization from each subject (see Form 7), unless a waiver of HIPAA authorization has been completed and submitted. (see Form 5).

C.3. For each of the boxes checked in 1, how were the original data, records, or human biological specimens collected? Describe the process of data collection including consent, if applicable.

C.4. For each of the boxes checked in 1, where do these data, records or human biological specimens currently reside?

C.5. For each of the boxes checked in 1, do you have permission from the custodians of the data, records or human biological specimens (e.g., pathology dept, tissue bank, original researcher)? Include data use agreements, if required by the custodian of data that are not publicly available.

C.6. If the research involves human biological specimens, has the purpose for which they were collected been met before removal of any excess? For example, has the pathologist in charge or the clinical laboratory director certified that the original clinical purpose has been satisfied? Explain if necessary.

__ yes  __ no  __ not applicable (explain)

C.7. Do all of these data, records or specimens exist at the time of this application? If not, explain how prospective data collection will occur.

__ yes  __ no  If no, explain
This application is to seek renewal or to report closure of a human subjects research project that has been approved by the IRB. All studies require continuing IRB review at intervals appropriate to the degree of risk, but at least once per year. Conducting human subject research without current IRB approval is a violation of federal and institutional regulations. *If IRB approval of a project expires prior to the renewal of approval by the IRB, it is considered a lapsed study and all research-related procedures must halt, except where doing so would jeopardize the welfare of the human subjects.*

*If the study involving Human Subjects Research has ended:*
- Complete and submit only the progress report (i.e., *Conflict of Interest page is inapplicable*).

*If the research is continuing:*
- Include the items identified in the checklist, next page.

**Submission Instructions**

This form is in Word format.
- Click into the highlighted area ( ) requesting an answer and type your answers into the form.
- Save the form.
- Send the application and all other pertinent documentation (ie protocol, informed consent, etc.) electronically as a pdf via email to irb@centrahealth.com.

**Address for all Applications and Other Correspondence**

irb@centrahealth.com electronically
If the research is continuing:
• Check the relevant items.

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<th>Check</th>
<th>Item</th>
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<tr>
<td>□ 1</td>
<td>This form (renewal/update or closure).</td>
</tr>
<tr>
<td>□ 2</td>
<td>Any items specifically requested in questions # 4 through 9 (in that order).</td>
</tr>
<tr>
<td>□ 3</td>
<td>This application should be updated to include any modifications since the study was initially approved or last renewed. If there are any new modifications included with this renewal, highlight the proposed modifications by underlining.</td>
</tr>
<tr>
<td>□ 4</td>
<td>Clean copies of all consent document(s) to be used in the upcoming approval period, for stamping, if applicable. ICF are only required if there are changes to the ICF.</td>
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Centra IRB study #: ____________ IRB of Record: ____________ Date: ____________

Title of Study: __________________________

Principal Investigator: __________________________ Study Coordinator: __________________________

For industry sponsored research (if applicable):
Sponsor’s master protocol version #: ____________ Version date: ____________
Investigator Brochure version #: ____________ Version date: ____________
IND (Investigational New Drug) #: ____________ IDE (Investigational Device Exemption #: ____________
Any other details you need documented on IRB approval: ____________

1. In a few sentences, describe the past year’s work, and describe what you plan for the upcoming year, including data analysis, if relevant.

2. Number of subjects involved through direct contact or use of their data (Note: b+d should not be larger than a)
   a. Total local projected number as approved by IRB:
   b. Total number of subjects involved to date locally (for clinical trials include “screen failures”):
   c. Number of subjects added since last renewal locally:
   d. Number to be included in upcoming year locally:
   e. Total enrollment for the study:
**Appendix D: Centra Health IRB Renewal or Closure of Human Subjects Research Version 9 17MAR2020**

Answer the following questions based on information since initial approval or last renewal. Only include subjects covered by this IRB.

<table>
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<th>Question</th>
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<tr>
<td>3. Have there been any modifications approved since the last review? If your IRB application has not already been updated to reflect these changes, do so now and attach any revised documents, including application and/or consent documents. (Not required for updates.)</td>
<td>__ yes __ no</td>
</tr>
<tr>
<td>4. Have any local subjects withdrawn voluntarily or been withdrawn from the study? __ yes, explain: give number and reasons for withdrawals.</td>
<td>__ yes __ no</td>
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<tr>
<td>5. Have there been any complaints about the research from local subjects or others? __ yes, explain</td>
<td>__ yes __ no</td>
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<tr>
<td>6. Have there been any findings (e.g., publications, new information) that alter the risk/benefit ratio or otherwise impact the study? __ yes, explain, including whether these new findings are relevant to participants’ willingness to continue.</td>
<td>__ yes __ no</td>
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<td>7. Have there been any relevant multi-center reports? __ yes, provide a copy of the report.</td>
<td>__ yes __ no</td>
</tr>
<tr>
<td>8. Does this study have a Data and Safety Monitoring Committee (DSMC or DSMB)? __ yes, provide a report from the DSMC.</td>
<td>__ yes __ no</td>
</tr>
<tr>
<td>9. Have there been local unanticipated problems or serious adverse events that have not previously been submitted to the IRB? __ yes, include all appropriate copies. If copies have been sent to the IRB in the past, please note the date(s) of the letter to the IRB.</td>
<td>__ yes __ no</td>
</tr>
<tr>
<td>10. Has this study been audited by external sponsor or monitor since approved or last renewed? __ yes, include a copy of the audit report.</td>
<td>__ yes __ no</td>
</tr>
<tr>
<td>11. Are you requesting any changes to the study or consent documents? __ yes, include the form requesting Modification of Approved Human Subjects Research and underline the proposed change in the updated application and/or consent documents. (Not required for updates.)</td>
<td>__ yes __ no</td>
</tr>
<tr>
<td>12. Studies that involve surveying employees require Human Resource approval which must be obtained prior to application submission to the IRB. The contact for the Human Resource Department is HR Director at 434-200-5342.</td>
<td></td>
</tr>
</tbody>
</table>

**Action requested by Principal Investigator (choose only one):**

- **Renew approval:**
  - Study has always involved only analysis of existing data or specimens. Continue as approved.
  - Study involves(ed) direct interaction/intervention or contact with subjects:
    - Continue as approved: Enrollment of new subjects continues.
    - Enrollment of new subjects closed; interaction/intervention with previously enrolled subjects continues.
    - Direct interaction with subjects completed but subsequent monitoring or follow up continues.
    - Subjects’ involvement completed but renewal is requested for data analysis.

- **Closure of Study:**
  - Research completed: Identifiable data or human biological specimens are stored according to plan already approved by the IRB.
  - Research completed: All data or human biological specimens are deidentified.
  - Lack of funding or other (specify):

---

Signature of Principal Investigator ___________________________ Date __________

Typing my name on the line above constitutes an electronic signature.
Centra Institutional Review Board  
Conflict of Interest Questions and Certification

The following questions apply to **all IRB Principal Investigators and/or Study Doctors and Study Coordinators** engaged in the design, conduct, or reporting results of this project **and/or Related Party**.

**Definitions:**

**Related Party** is the Principal Investigator’s and/or Study Doctor and Study Coordinator’s spouse, domestic partner, or dependent children, siblings, parents or equivalents by marriage, or other individuals residing in the PI/Study Coordinator’s household.

**Financial Interest:** Anything of monetary value received from a financially interested company, including but not limited to: director’s fees; consulting fees; honoraria; gifts; other emoluments or “in kind” compensation such as travel and entertainment (including those from a third party if the original source is a financially interested company), for any services not directly related to the reasonable costs of conducting the research as specified in the research agreement; equity interest (e.g., stocks, stock options, convertible notes, other ownership interests); and intellectual property rights (e.g., license fees, current and future royalties from patents and copyrights).

The term “Financial Interest” does not include:

i. Salary or other remuneration received from [Hospital];

ii. Holdings in mutual funds;

iii. De minimus gifts whose aggregate value does not exceed $100 per annum; or reasonable business expenses, including travel and meals provided in the regular course of business.

**Conflict of Interest:** means any situation or circumstance in which an IRB Member or a Related Party has a financial, personal, or other interest (including, but not limited to, an Individual Interest, Financial Interest, or Institutional Interest) which conflicts with, compromises, or has the appearance of conflicting with or compromising the individual’s independent judgment and objectively rendering the member incapable of making an unbiased and objective decision regarding the research.

<table>
<thead>
<tr>
<th>A.3.1. Currently or during the term of this research study, does any member of the research team or a Related Party have or expect to have:</th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>(a) A personal financial interest in or personal financial relationship (including gifts of cash or in-kind) with the sponsor of this study? Explain:</td>
<td>__ yes __ no</td>
<td></td>
</tr>
<tr>
<td>(b) A personal financial interest in or personal financial relationship (including gifts of cash or in-kind) with an entity that owns or has the right to commercialize a product, process or technology studied in this project? Explain:</td>
<td>__ yes __ no</td>
<td></td>
</tr>
<tr>
<td>(c) A personal financial interest in or personal financial relationship (including</td>
<td>__ yes __ no</td>
<td></td>
</tr>
</tbody>
</table>
gifts of cash or in-kind) with an entity engaged in the performance of this project as a subcontractor, sub-recipient or vendor?

Explain: _________________________________________________________
________________________________________________________________
________________________________________________________________

(d) A board membership of any kind or an executive position (paid or unpaid) with the sponsor of this study or with an entity that owns or has the right to commercialize a product, process or technology studied in this project?

Explain: _________________________________________________________
________________________________________________________________
________________________________________________________________

A.3.2. Has Centra Health or has a Centra Health-related foundation received a cash or in-kind gift from the sponsor of this study for the use or benefit of any member of the research team?

Explain: _________________________________________________________
________________________________________________________________
________________________________________________________________

A.3.3. Has Centra Health or has a Centra Health-related foundation received a cash or in-kind gift for the use or benefit of any member of the research team from an entity that owns or has the right to commercialize a product, process or technology studied in this project?

Explain: _________________________________________________________
________________________________________________________________
________________________________________________________________

If the answer to ANY of the questions above is yes, list name(s) of all research team members for whom any answer to the questions above is yes:

________________________________________________________________

Certification by Principal Investigator/Study Doctor/Study Coordinator. By submitting this IRB application, I (the PI/Study Doctor/Study Coordinator) certify that the information provided above is true and accurate regarding my own circumstances, that I have inquired of every Centra Health employee who will be engaged in the design, conduct or reporting of results of this project as to the questions set out above, and that I have instructed any such person who has answered “yes” to any of these questions to complete and submit for approval a Conflict of Interest Evaluation Form. I understand that as Principal Investigator I am obligated to ensure that any potential Conflicts of Interest that exist in relation to my study are reported as required by IRB policy.
Signature of Principal Investigator  
Typing my name on the line above constitutes an electronic signature.

_________________________  ________________________
Signature of Study Coordinator  Date
Typing my name on the line above constitutes an electronic signature.
This application is to seek approval for a modification to a currently approved study. Any proposed changes to previously approved human subjects research must be reviewed and approved by the IRB prior to implementation. This includes modifications to the study, inclusion or exclusion criteria, recruitment methods, research personnel, or any new or revised study materials. If the modifications reported relate to or implicate a Related Party, Financial Interest or potential Conflict of Interest, the Conflict of Interest Questions and Certification attached here must be completed. Approval is required for all modifications whether initiated by the investigator or external sponsor. This form should not be used to report violations and deviations.

Instructions for Submitting

Include with your submission the items indicated in the list on the next page, where applicable.

Submission Instructions
This form is in Word format.
- Click into the highlighted area ( ) requesting an answer and type your answers into the form.
- Save the form.
- Send the application and all other pertinent documentation (ie protocol, informed consent, etc.) electronically as a pdf via email to irb@centrahealth.com.

Address for all Applications and Other Correspondence

irb@centrahealth.com electronically
Include the items indicated, where applicable:

- **Check** the relevant items below and include one copy of all checked items 1-5 in the order listed.

  → Applications will be returned if these instructions are not followed.

<table>
<thead>
<tr>
<th>Check</th>
<th>Item</th>
</tr>
</thead>
<tbody>
<tr>
<td>□</td>
<td>1. A concise summary of the requested modification using this form. List and describe each proposed change to aid in IRB review. Add pages as necessary. Provide a concise summary of changes when submitting an updated Investigator Brochure or Master Protocol.</td>
</tr>
<tr>
<td>□</td>
<td>2. New or revised consent forms, questionnaires, surveys, recruitment materials, advertisements, etc.</td>
</tr>
<tr>
<td>□</td>
<td>3. If you have made substantive changes to the study design or procedures, submit a revised full IRB application with changes highlighted by underlining.</td>
</tr>
<tr>
<td>□</td>
<td>4. The sponsor's document describing the amendment, if any.</td>
</tr>
<tr>
<td>□</td>
<td>5. If adding personnel, include name, location (Centra Health or specific outside location), role, and email address for each person who should receive electronic copies of IRB correspondence to PI.</td>
</tr>
</tbody>
</table>

**IRB study #:**

**IRB of Record:** ______________

**Date:**

**Title of Study:**

**Principal Investigator:**

**Study Coordinator:**

(if applicable)

**For industry sponsored research (if applicable):**

- Sponsor’s master protocol version #: Version date:
- Investigator Brochure version #: Version date:
- IND (Investigational New Drug) #: IDE (Investigational Device Exemption #:)

Any other details you need documented on IRB approval:

1. **List and describe each proposed change:**

2. **Is this modification being submitted in response to an unanticipated problem/adverse event or new findings?**  
   _yes_  _no_  
   If yes, explain, including whether these events or findings are relevant to participants’ willingness to continue.

3. **Do any of the proposed changes increase risk?**  
   _yes_  _no_  
   If yes, explain.

---

Signature of Principal Investigator

Typing my name on the line above constitutes an electronic signature.

---

Appendix E: Centra Health IRB Modification of Approved Human Subjects Research Version 7 17MAR2020
Centra Institutional Review Board
Conflict of Interest Questions and Certification

The following questions apply to **all IRB Principal Investigators and/or Study Doctors and Study Coordinators** engaged in the design, conduct, or reporting results of this project **and/or Related Party**.

**Definitions:**

**Related Party** is the Principal Investigator’s and/or Study Doctor and Study Coordinator’s spouse, domestic partner, or dependent children, siblings, parents or equivalents by marriage, or other individuals residing in the PI/Study Coordinator’s household.

**Financial Interest:** Anything of monetary value received from a financially interested company, including but not limited to: director’s fees; consulting fees; honoraria; gifts; other emoluments or “in kind” compensation such as travel and entertainment (including those from a third party if the original source is a financially interested company), for any services not directly related to the reasonable costs of conducting the research as specified in the research agreement; equity interest (e.g., stocks, stock options, convertible notes, other ownership interests); and intellectual property rights (e.g., license fees, current and future royalties from patents and copyrights).

The term “Financial Interest” does not include:

- i. Salary or other remuneration received from [Hospital];
- ii. Holdings in mutual funds;
- iii. De minimus gifts whose aggregate value does not exceed $100 per annum; or reasonable business expenses, including travel and meals provided in the regular course of business.

**Conflict of Interest:** means any situation or circumstance in which an IRB Member or a Related Party has a financial, personal, or other interest (including, but not limited to, an Individual Interest, Financial Interest, or Institutional Interest) which conflicts with, compromises, or has the appearance of conflicting with or compromising the individual’s independent judgment and objectively rendering the member incapable of making an unbiased and objective decision regarding the research.

<table>
<thead>
<tr>
<th>A.3.1.</th>
<th>Currently or during the term of this research study, does any member of the research team or a Related Party have or expect to have:</th>
</tr>
</thead>
<tbody>
<tr>
<td>(a)</td>
<td>A personal financial interest in or personal financial relationship (including gifts of cash or in-kind) with the sponsor of this study?</td>
</tr>
<tr>
<td>Explain:</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>__ yes __ no</td>
</tr>
<tr>
<td>(b)</td>
<td>A personal financial interest in or personal financial relationship (including gifts of cash or in-kind) with an entity that owns or has the right to commercialize a product, process or technology studied in this project?</td>
</tr>
<tr>
<td>Explain:</td>
<td></td>
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<tr>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>__ yes __ no</td>
</tr>
</tbody>
</table>
| (c)    | A personal financial interest in or personal financial relationship (including gifts of cash or in-kind) with an entity engaged in the performance of this project as a subcontractor, sub-
|        | recipient or vendor?                                                                                                               |
| Explain: |                                                                                                                                     |
|        |                                                                                                                                     |
|        | __ yes __ no                                                                                                                      |
| (d)    | A board membership of any kind or an executive position (paid or unpaid) with the sponsor of this study or with an entity that owns or has the right to commercialize a product, |
|        |                                                                                                                                     |
|        | __ yes __ no                                                                                                                      |

Appendix E: Centra Health IRB Modification of Approved Human Subjects Research Version 7 17MAR2020
process or technology studied in this project?

Explain: _________________________________________________________
________________________________________________________________
________________________________________________________________

<table>
<thead>
<tr>
<th>A.3.2.</th>
<th>Has Centra Health or has Centra Health-related foundation received a cash or in-kind gift from the sponsor of this study for the use or benefit of any member of the research team?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>__ yes __       no</td>
</tr>
</tbody>
</table>

Explain: _________________________________________________________
________________________________________________________________
________________________________________________________________

<table>
<thead>
<tr>
<th>A.3.3.</th>
<th>Has Centra Health or has a Centra Health-related foundation received a cash or in-kind gift for the use or benefit of any member of the research team from an entity that owns or has the right to commercialize a product, process or technology studied in this project?</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>__ yes __       no</td>
</tr>
</tbody>
</table>

Explain: _________________________________________________________
________________________________________________________________
________________________________________________________________

If the answer to ANY of the questions above is yes, list name(s) of all research team members for whom any answer to the questions above is yes:

Certification by Principal Investigator/Study Doctor/Study Coordinator. By submitting this IRB application, I (the PI/Study Doctor/Study Coordinator) certify that the information provided above is true and accurate regarding my own circumstances, that I have inquired of every Centra Health employee who will be engaged in the design, conduct or reporting of results of this project as to the questions set out above, and that I have instructed any such person who has answered “yes” to any of these questions to complete and submit for approval a Conflict of Interest Evaluation Form. I understand that as Principal Investigator I am obligated to ensure that any potential Conflicts of Interest that exist in relation to my study are reported as required by IRB policy.

__________________________  __________________________
Signature of Principal Investigator  Date  
Typing my name on the line above constitutes an electronic signature.

__________________________  __________________________
Signature of Study Coordinator  Date  
Typing my name on the line above constitutes an electronic signature.
This application is to report correspondence or progress to a currently approved study. Ie: report is requested more frequent than annually.

Instructions for Submitting

Include with your submission the items indicated in the list on the next page, where applicable.

Submission Instructions
This form is in Word format.
- Click into the highlighted area ( ) requesting an answer and type your answers into the form.
- Save the form.
- Send the application and all other pertinent documentation (ie protocol, informed consent, etc.) electronically as a pdf via email to irb@centrahealth.com.

Address for all Applications and Other Correspondence

irb@centrahealth.com electronically
Centra HEALTH Institutional Review Board

REPORT OF APPROVED HUMAN SUBJECTS RESEARCH

Version 4 17MAR2020

IRB study #: ___________________________ Date: ___________________________

IRB of Record: ___________________________ Date: ___________________________

Title of Study: ___________________________ Date: ___________________________

Continuing Review

1. Number of local subjects accrued since last report and total.

2. Summary of any unanticipated problems.

3. Summary of adverse events. Did they occur at the expected frequency and level of severity as documented in the research protocol, the informed consent document, and the investigator brochure?

4. Summary of circumstances that lead to the withdrawal of any local subjects.

5. Summary of any local complaints about the research.

6. Summary of any new literature that is relevant to the research.

7. Review of any amendments or modifications to the research since the last report, any modifications to the protocol previously approved.

8. Copies of any revised consent documents since the last local review.

9. Summary of currently available study-wide adverse events and/or interim findings and monitoring entity’s assessment of the information reviewed.

10. Other: ___________________________

Principal Investigator: ___________________________ Study Coordinator: ___________________________

(if applicable)

For industry sponsored research (if applicable):

  Sponsor’s master protocol version #: ___________________________ Version date: ___________________________
  Investigator Brochure version #: ___________________________ Version date: ___________________________
  IND (Investigational New Drug) #: ___________________________ IDE (Investigational Device Exemption #: ___________________________

Any other details you need documented on IRB approval:

________________________________________________________
Signature of Principal Investigator

Typing my name on the line above constitutes an electronic signature.

____________________________
Date
Use this form if you need to access and use only the minimum amount of PHI necessary to review eligibility criteria and contact potential subjects.

**Instructions for Submitting**

Include with your submission the items indicated in the list on the next page, where applicable.

**Submission Instructions**

This form is in Word format.

- Click into the highlighted area ( ) requesting an answer and type your answers into the form.
- Save the form.
- Send the application and all other pertinent documentation (ie protocol, informed consent, etc.) electronically as a pdf via email to irb@centrahealth.com.

**Address for all Applications and Other Correspondence**

irb@centrahealth.com electronically
Date: __________________________  IRB of Record: ____________

Principal Investigator: _______________________________________________________

Email address: ______________________________________________________________

Phone number: __________________________________________________________________

Research Staff needing access to protected health information:
(As approved by IRB in Application Section A)

Study Title: ___________________________________________________________________

Number of records needed:  □ > 50  □ ≤ 50

The Centra Institutional Review Board (Federal Assurance Number __________ Exp: __________) may waive or alter the requirement to obtain authorization from research subjects in order to use or disclose their protected health information, provided that the investigator justifies, and the IRB agrees, that specific criteria have been met. Please explain how your research study meets the criteria by answering each of the following questions:

1. In this study, how does the use of disclosure of protected health information involve no more than minimal risk to privacy of the subjects?

________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

2. What is your plan to protect identifiable health information from improper use and disclosure?

________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

3. What is your plan to destroy the identifiers? Include how and when.

________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

4. Why is it not practical to obtain an authorization from subjects?

________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

5. Can the research be done without the protected health information? If not, why not?

________________________________________________________________________________
________________________________________________________________________________
________________________________________________________________________________

☐ I am requesting access to PHI without authorization for the following reason:

☐ identify potential subjects

☐ use or disclose minimum information during the course of my investigation.

Centra Health IRB Protected Health Information Waiver of Authorization Version 5 17MAR2020
6. Please complete the following to describe selection criteria for records required; the dates of the records required; and data fields required for the research.

   a. Selection Criteria for records required
   b. Dates of required records: from ___/___/___ through ___/___/___
   c. Data fields required (list fields required from an electronic data base, or list fields to be recorded from the paper record by the researcher)
   d. Anticipated sources of information (check all that apply)
      □ Paper medical records
      □ Electronic files
      □ Other ________________

By submitting this form to the Centra IRB, the PI attests to the following:

I declare that the requested information constitutes the minimum necessary data to accomplish the goals of the research.

I agree that the protected health information will not be re-used or disclosed to any other person or entity, except as required by law, for the authorized oversight of the research study, or for other research for which the use or disclosure of protected health information would be permitted by the Privacy Regulation (45 CFR 164.512)

Signature of PI: ____________________________ Date: ________________
Typing my name on the line above constitutes an electronic signature.

FOR IRB USE ONLY

IRB # ____________

On the date noted below, as prescribed by the Privacy Rule of the Health Insurance Portability and Accountability Act of 1996 [HIPAA], Centra IRB approved an alteration or waiver of authorization for the use and disclosure of protected health information in the above entitled study. The Centra IRB determined that the alteration or waiver, in whole or in part, of authorization satisfies the above criteria as indicated. This application was reviewed and approved under full convened board procedures at 45 CFR 46.108(b) or expedited review procedures at 45 CFR 46.110.

Full Board Review or Exempt Review (CIRCLE) Date: ___/___/___

Signature: __________________________________________
Typing my name on the line above constitutes an electronic signature.

Print Name: ________________________________
This Exempt Research Checklist (ERC) application is to determine if your research requires submission of an application to Centra Health Institutional Review Board.

If the ONLY involvement of human subjects will be in one or more of the following categories listed in this document AND all the answers in one or more categories are “True” (except as noted in statements 7 and 11 below), the research may be eligible for exemption. However, the research must be determined to be exempt by the IRB.

**Supplemental documentation is required for consideration of exemption status. A submission checklist (Appendix A) is attached to assist you.**

Complete and send the application and all other pertinent electronically as a pdf via email

Officeofresearch@centrahealth.com

**Address for all Applications and Other Correspondence**

Officeofresearch@centrahealth.com electronically
Centra Research/EBP/QI/PI Project

Algorithm

IF you are a student:
Contact the Office of Medical Education and Student Affairs
(434) 200-5255

Obtain IRB approval from University, if applicable

Contact: Dr. Vicky Brunet, DNP, NNP-BC, CCRN
e-mail: Vicky.brunet@Centrahealth.com
Director, Nursing Research
For Centra research process/IRB application instructions

Submit proposal to
OfficeofResearch@Centrahealth.com

All submissions except Centra RNs

Exempt IRB
Or
Full IRB, if applicable

Invitation to present to the Nursing Research Council

Centra Nurses

Nursing Research Council

Exempt IRB
Or
Full IRB, if applicable
Date: ____________

Centra IRB #: ___________ (will be assigned by the IRB upon submission)

IRB of Record ________________

Facility:

Principal Investigator:

Email address:

Phone number:

Title of Research Project/Study Title:

Please read the following to answer the question below:
Do the HHS regulations for the protection of human subjects in research (45 CFR part 46) apply to quality improvement activities conducted by one or more institutions whose purposes are limited to: (a) implementing a practice to improve the quality of patient care, and (b) collecting patient or provider data regarding the implementation of the practice for clinical, practical, or administrative purposes?

No, such activities do not satisfy the definition of "research" under 45 CFR 46.102(d), which is "...a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge..." Therefore, the HHS regulations for the protection of human subjects do not apply to such quality improvement activities, and there is no requirement under these regulations for such activities to undergo review by an IRB, or for these activities to be conducted with provider or patient informed consent.

Having read the above,

1. Is this research? If yes, stop and complete the initial application Form 1.

2. Is this quality improvement activities? If yes and you anticipate publication, please indicate here □ and continue to fill out the form.

Supplemental documentation is required for consideration of exemption status.

<table>
<thead>
<tr>
<th>Criteria that must be met for the research to be determined to be consistent with IRB ethical standards.</th>
<th>True</th>
<th>Not True</th>
</tr>
</thead>
<tbody>
<tr>
<td>The research holds no more than minimal risk to subjects.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Selection of subjects is equitable.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>If there is recording of identifiable information, there are adequate provisions to maintain the confidentiality of the data.</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
There are adequate provisions to maintain the privacy interests of subjects.

<table>
<thead>
<tr>
<th>Checklist Statements</th>
<th>True</th>
<th>Not True</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Category 1 – For Educational Settings</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1. The research will only be 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.)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2. The research will involve only normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>3. The research will not involve individuals as participants who are known to be prisoners.</td>
<td></td>
<td></td>
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<tr>
<td>4. The research is not subject to FDA regulations.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Category 2 – For Educational Tests, Surveys, Interviews, Public Behavior Observation:</strong></td>
<td></td>
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</tr>
<tr>
<td>5. The research will involve only the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior.</td>
<td></td>
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<tr>
<td>Address statement 6 only if the research will involve children as participants. If children will NOT participate, state N/A and continue with statement 7.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6. The procedures will be limited to the use of educational tests (cognitive, diagnostic, aptitude, achievement) or observation of public behavior where the investigator will NOT participate in the activities being observed.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>7. The information obtained from educational tests, survey procedures, interview procedures or observation of public behavior will be recorded in such a manner that human subjects CANNOT be identified, directly or through identifiers linked to the subjects. “True” to either statement 7 or 8 will qualify for exemption provided that statements 9 and 10 are true.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>8. Any disclosure of the human subjects’ responses outside the research could NOT reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, or reputation.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>9. The research will not involve individuals as participants who are known to be prisoners.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>10. The research is not subject to FDA regulations.</td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Category 3 – For Educational Tests, Surveys, Interviews, Public Behavior Observation of Public Officials:</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>11. The research will involve only the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior AND the human subjects are 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.) “True” to either statement 11 or 12 will qualify for exemption provided that statements 13 and 14 are true.</td>
<td></td>
<td></td>
</tr>
<tr>
<td>12. The research will involve only the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior AND federal statute(s)</td>
<td></td>
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</tr>
</tbody>
</table>
require without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

13. The research will **not** involve individuals as participants who are known to be prisoners.

14. The research is not subject to FDA regulations.

**Category 4 – For Existing Data, Documents and Specimens:**

15. The research will 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 the IRB to determine whether the research is exempt. All materials to be reviewed currently exist at the time of this exemption request.)

16. The sources of the existing data, documents, records or specimens are publicly available **OR** the information will be recorded by the investigator in such a manner that participants cannot be readily identified either directly or through identifiers (such as a code) linked to them.

17. The research will **not** involve individuals as participants who are known to be prisoners.

18. The research is not subject to FDA regulations.

**Category 5 – For Public Benefit or Service Programs (Federal):**

19. The project is a research or demonstration project conducted by or subject to the approval of a (federal) Department or Agency head and which 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 public benefit or service programs.

20. The research will **not** involve individuals as participants who are known to be prisoners.

21. The research is not subject to FDA regulations.

22. The program under study delivers a public benefit (e.g., financial or medical benefits as provided under the Social Security Act) or service (e.g., social, supportive, or nutrition services as provided under the Older Americans Act).

23. The research or demonstration project will be conducted pursuant to specific federal statutory authority.

24. There is no statutory requirement that the project be reviewed by an IRB.

25. The project does not involve significant physical invasions or intrusions upon the privacy of participants.

26. The exemption has authorization or concurrence by the funding agency.

**Category 6 – For Taste and Food Quality and Consumer Acceptance Studies:**

27. The research involved only a taste and food quality evaluations or a food consumer acceptance study in which (i) wholesome foods without additives will be consumed **OR** (ii) food will be consumed that contains a food ingredient, agricultural chemical or environmental contaminant that is at or below the level found to be safe by the Food and Drug Administration or is approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture.
28. The research will **not** involve individuals as participants who are known to be prisoners.

**Emergency Use of an Unapproved Test Article (i.e., a drug, device or biologic that is not FDA-Approved)**

The activity involves emergency use of an investigational drug, device or biologic. Such an activity is not exempt from IRB review. However, this emergency use may occur prior to IRB review and approval (see Category A and B in the Emergency Use Policy for details.) Note that such an emergency use must be reported to the IRB within five business days.

The activity does not meet with DHHS definition of “research.”

Signature of Principal Investigator:

______________________________________________________________

Typing my name on the line above constitutes an electronic signature.

Printed Name

________________________________________________________________

Date __________________

**FOR THE IRB REVIEWER ONLY:**

Is the activity exempt? YES [   ] NO [   ]

Does the research meet the standards of ethical conduct? YES [   ] NO [   ]

Which exemption category or categories apply to the activity?

1/2/3/4/5/QI/PI/EBP

Approved by IRB Exempt Committee (date): __________________________

Signature of IRB Reviewer:

________________________________________________________________

Typing my name on the line above constitutes an electronic signature.

Printed Name

________________________________________________________________

Date ___________________________________
EXEMPT SUBMISSION CHECKLIST

__________ Letter of support from Unit Manager (if applicable)

__________ Primary Investigator’s resume

__________ All educational materials for staff and patients (if applicable)

__________ Research or EBP project proposal form

__________ Data collection tools/instruments (surveys, etc.)

__________ Any additional subject information materials

__________ Any other pertinent documents related to this study
You must have each participant sign this form if your study will use Protected Health Information (PHI) [e.g., existing data, records or specimens (including electronic information from a clinical database)].

**Instructions for Submitting**

Include a sample of your form with your submission.

**Submission Instructions**

This form is in Word format.

- Click into the highlighted area ( ) requesting an answer and type your answers into the form.
- Save the form.
- Send the application and all other pertinent documentation (ie protocol, informed consent, etc.) electronically as a pdf via email to irb@centrahealth.com.

**Address for all Applications and Other Correspondence**

[irb@centrahealth.com](mailto:irb@centrahealth.com) electronically
During the research study, your doctors, their staff, their agents and hospital personnel (collectively called the “Researchers”) will be collecting health information about you that is called “protected health information” or “PHI.” PHI is protected under a federal privacy law called the Health Insurance Portability and Accountability Act (HIPAA) (45 C.F.R. Parts 160 and 164). By signing this form, you are giving your written permission for the Researchers, as well as the study Sponsor [INSERT SPONSOR NAME] and the Sponsor’s agents and contractors (collectively called the “Sponsor Group”) to use and disclose (share) your PHI for the purposes described below:

1. These are the types of your PHI that may be used and shared in the study:
   - [State PHI elements that will be used and shared, e.g., name, gender, initials, address, telephone number, date of birth, dates of hospitalization, social security number and insurance information;]
   - All information in your medical record, the results of physical exams and tests, your medical history and other data collected during the study;
   - Insurance reimbursement information (e.g., bills for hospital care, physicians services, laboratory tests, diagnostic procedures, drugs, etc.); and
   - Information contained in your medical records prepared by other healthcare providers from whom you have sought medical care while taking part in the study.

2. The Researchers may:
   - [State how Researchers will use and disclose PHI, e.g., Receive, use and share your PHI to conduct the study;]
   - Share your PHI with the Sponsor Group;
   - Share your PHI, as required by law, and with representatives of government organizations, review boards, including the [Insert Institution Name] IRB, and
others who are required to watch over the safety and effectiveness of medical products or the conduct of medical research; and

• Remove from your health information your name, and to the extent feasible, other information that could be used to identify you.]

3. The Sponsor Group may:

• [State how Sponsors will use and disclose PHI, e.g., Receive, use and share your PHI to conduct the study and as required by law;]

• Use and share your PHI as described in the Informed Consent form and in this Authorization;

• Use and share your insurance information (e.g., hospital and doctor bills, bills for laboratory test, diagnostic procedures, drugs, etc.) for reimbursement purposes;

• Share your PHI with representatives of US and foreign government agencies, review boards and others who watch over the safety and effectiveness of medical products and research activities;

• Use and share your PHI for internal reference, for comparison with other data, to help design subsequent trials, and in regulatory papers submitted to United States and foreign regulatory agencies for later developed products; and

• Remove from your health information, your name, and to the extent feasible, other information that could be used to identify you.]

4. Please note:

• After your PHI is given to someone other than the Researchers, federal privacy laws might not protect the PHI from further use or disclosure. However, the Researchers and Sponsor Group will protect your PHI by using and disclosing it only as permitted by you in this Authorization.

• You do not have to sign this Authorization, but if you do not, you will not be able to be in the study if the study involves treatment.

• Your medical treatment, payment for services, enrollment and eligibility for benefits will not be based on whether or not you sign this Authorization.

• This Authorization will expire when the research ends, and all required study monitoring is concluded.

By signing this consent form, you authorize the use and disclosure of health information about you as described above. You have the right to revoke this authorization, in writing, at any time by sending written notification to [insert name and address]. If your revoke your authorization for use and disclosure of health information for research purposes, you will be discontinued from the
research. However, the principal investigator, hospital, sponsor and its researchers may still use and disclose health information that has already been obtained as permitted in this authorization to maintain the reliability of the research.

- If you withdraw this Authorization, your PHI that has already been shared may continue to be used and shared to maintain the integrity of the research.
- While the Study is taking place, you will not be allowed to see your health information that is created or collected during the study. After the study is finished; however, you may see this information if you ask your doctor, in writing.
- The results of the study may be published in scientific journals or presented at medical meetings, but your name and identify will not be disclosed in them.

**PATIENT’S HIPAA AUTHORIZATION**

By signing this Authorization form, I give my written permission for my Protected Health Information to be used and collected as described in this form. I have been given a copy of this signed Authorization.

_______________________________________________________/ ______________
Signature of Patient          Date

_______________________________________________________
Printed Name of Participant

**OR**

_______________________________________________________/ ______________
Signature of Legal Authorized Representative & their relationship  Date

_______________________________________________________
Printed name of Legal Authorized Representative & their relationship
Code of Federal regulations Title 21-Food and Drugs, Part 50—Protection of Human Subjects:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfcdr/CFRSearch.cfm?CFRPart=50&showFR=1
Appendix K

Code of Federal Regulations Title 21-Food and Drugs, Part 56-Institutional Review Boards:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfCfr/CFRSearch.cfm?CFRPart=56&showFR=1
Code of Federal Regulations Title 45—Public Welfare, Part 46—Protection of Human Subjects:
Information Sheet Guidance For
IRBs, Clinical Investigators, and
Sponsors

Significant Risk and Nonsignificant Risk
Medical Device Studies

Additional copies are available from:
Office of Good Clinical Practice
Office of Special Medical Programs, Office of the Commissioner
Food and Drug Administration
10903 New Hampshire Ave., WO32-5129
Silver Spring, MD 20993-5129
(Tel) (301)-796-8340

or

Division of Small Manufacturers, International, and Consumer Assistance
Office of Communication, Education and Radiation Programs
Center for Devices and Radiological Health
Food and Drug Administration
10903 New Hampshire Ave., WO66-4521
Silver Spring, MD 20993
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U.S. Department of Health and Human Services
Food and Drug Administration
Center for Devices and Radiological Health (CDRH)

January 2006
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I. INTRODUCTION

This guidance is intended to provide advice to sponsors, clinical investigators, and institutional review boards (IRBs) on how to determine the differences between significant risk and nonsignificant risk medical device studies. This document supersedes Significant Risk and Nonsignificant Risk Medical Device Studies (September 1998) Office of Health Affairs, Food and Drug Administration. This document was revised to update the list of examples of significant and nonsignificant risk devices, to clarify the IRB’s responsibilities when making the risk determination for investigational medical devices, and to make the guidance consistent with the Agency’s good guidance practices regulations (21 CFR 10.115).

FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities. Instead, guidances describe the Agency's current thinking on a topic and should be viewed only as recommendations, unless specific regulatory or statutory requirements are cited. The use of the word should in Agency guidances means that something is suggested or recommended, but not required.

II. BACKGROUND

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1 This guidance document was developed by the Good Clinical Practice Program in coordination with the Agency Centers.
The Investigational Device Exemptions (IDE) regulation (21 CFR 812) describes three types of device studies: significant risk (SR), nonsignificant risk (NSR), and exempt studies. In this guidance, we discuss the two types of studies that are subject to the IDE regulation – the SR and NSR studies. For information on studies that are exempt from the IDE regulation, see the Information Sheet Guidance entitled, “Frequently Asked Questions About Medical Devices.”

III. SIGNIFICANT RISK AND NON-SIGNIFICANT RISK DEVICE STUDIES

A. What is a Significant Risk Device Study?

Under 21 CFR 812.3(m), an SR device means an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

B. What is a Nonsignificant Risk Device Study?

An NSR device study is one that does not meet the definition for an SR device study.

C. Who Decides Whether A Device Study is SR or NSR?

Sponsors are responsible for making the initial risk determination and presenting it to the IRB. FDA is also available to help the sponsor, clinical investigator, and IRB in making the risk determination.2

Unless FDA has already made a risk determination for the study, the IRB must review the sponsor's SR or NSR determination for every investigational medical device study reviewed and modify the determination if the IRB disagrees with the sponsor. If FDA has already made the SR or NSR determination for the study, the agency's determination is final. FDA is available to help the IRB when making its risk determination. (Also, see section VII. “How does an IRB document the SR or NSR determination?”)

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2 See the guidance entitled, “Procedures for Handling Inquiries Regarding the Need for an Investigational Device Exemptions Application for Research Involving Medical Devices.” This guidance may be found at: www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm126598.
FDA is the final arbiter as to whether a device study is SR or NSR and makes the determination when an IDE is submitted to FDA or if asked by the sponsor, clinical investigator, or IRB. See 21 CFR § 812.2(b)(1)

D. What are the Major Differences Between SR and NSR Device Studies?

The major differences between SR and NSR studies are in the IDE approval process and in the sponsor’s record keeping and reporting requirements, as outlined below.

1. Significant Risk (SR) Device Studies

- SR device studies must follow all the IDE regulations at 21 CFR 812.
- SR device studies must have an IDE application approved by FDA before they may proceed.

2. Nonsignificant Risk (NSR) Device Studies

- NSR device studies must follow the abbreviated requirements at 21 CFR 812.2(b).
- These abbreviated requirements address labeling, IRB approval, informed consent, monitoring, records, reports, and prohibition against promotion. However, there is no need to make progress reports or final reports to FDA.
- NSR device studies do not have to have an IDE application approved by FDA.
- Sponsors and IRBs do not have to report the IRB approval of an NSR device study to FDA. This means that an IRB may approve an NSR device study and an investigator may conduct the study without FDA knowing about it.
- An IRB’s NSR determination is important because the IRB serves as the FDA’s surrogate for review, approval, and continuing review of the NSR device studies. An NSR device study may start at the institution as soon as the IRB reviews and approves the study and without prior approval by FDA.

IV. WHAT ARE THE SPONSOR'S RESPONSIBILITIES WHEN INITIATING A DEVICE STUDY?

A. For Nonsignificant Risk Device Studies

- If the sponsor identifies a study as NSR, the sponsor must provide the reviewing IRB an explanation of its determination (21 CFR 812.2(b)(1)(ii)) and should provide any other information that may help the IRB in evaluating the risk of the study. For example, a
description of the device, reports of prior investigations with the device, the proposed investigational plan, subject selection criteria, and other information the IRB may need.

- If FDA has determined that the study is NSR, the sponsor should so inform the IRB. By providing such risk determination information to the IRB, the IRB’s workload should be reduced and the review process should be facilitated.

**B. For Significant Risk Device Studies**

- The sponsor must submit an IDE application to FDA and obtain the agency’s approval of the study. (See 21 CFR 812.20(a)(1) and (2))

- The sponsor must advise its clinical investigators about the SR status and obtain their agreement to comply with the applicable regulations governing such studies (i.e., 21 CFR Parts, 50, 56, 812) (See 21 CFR 812.43(c)(4)(i)). Sponsors should provide the IDE number and/or a copy of the IDE approval letter to the IRB when requested.

- Sponsors may send their SR device study to an IRB for review before the IDE application is approved by FDA. However, FDA cautions that an SR device study may not begin until FDA approves the IDE.

**V. WHAT ARE THE IRB’S RESPONSIBILITIES WHEN IT RECEIVES A DEVICE STUDY FOR REVIEW?**

- IRBs should have standard operating procedures that explain how the IRB makes SR and NSR determinations and that the decision should be documented. FDA considers this determination to be part of the IRB’s responsibilities for conducting its initial review of a study. (See 21 CFR 56.108)

- IRBs should make the SR or NSR determination about a study by reviewing relevant information at a convened meeting. This information includes the description of the device, reports of prior investigations conducted with the device, the proposed investigational plan, and subject selection criteria. The sponsor should provide the IRB with a risk assessment and the rationale used in making its SR or NSR determination.

- An IRB may agree or disagree with the sponsor’s initial NSR assessment.

- If the IRB determines the study is NSR, the IRB may approve the study using the criteria at 21 CFR 56.111. The study may begin without submission of an IDE application to FDA.

- If the IRB disagrees with the sponsor’s NSR assessment and decides the study is SR, the IRB must tell the clinical investigator, and where appropriate, the sponsor. (See 21 CFR 812.66)
• An IRB may approve the study as an SR device study, but the study may not begin until FDA approves the sponsor’s IDE application.

• To facilitate the IRB’s review of the study, an IRB may ask the sponsor for proof (i.e., a copy of FDA’s approval or conditional approval letter) that an SR study has an FDA-approved IDE application.

• The IRB should document its SR/NSR determination in the IRB meeting minutes.

VI. WHAT SHOULD IRBS CONSIDER WHEN MAKING THE SR AND NSR DETERMINATION?

• *What is the basis for the risk determination?* The risk determination is based on the proposed use of a device in an investigation, and not on the device alone.

• *What is the nature of harm that may result from use of the device?* SR studies are those that present a potential for serious risk to the health, safety, or welfare of a subject. See the question “What is a Significant Risk Device Study?” for further information.

• *Will the subject need to undergo an additional procedure as part of the investigational study, for example, a surgical procedure?* IRBs should consider the potential harm the procedure could cause as well as the potential harm caused by the device. Several examples follow:

1. The study of a change to a commercially available pacemaker (e.g., new leads, battery pack, or software) poses an SR because the device is used to support or sustain human life and it presents a potential for serious harm to the subjects. This is true even though the changed pacemaker may potentially pose less risk, or only slightly greater risk, in comparison to the commercially available model.

2. The study of an extended wear contact lens is SR because wearing the lens continuously overnight while sleeping presents a potential for injuries not normally seen with daily wear lenses, which are NSR.

3. An investigational study of a sensor pad to find out if the device can detect the electrical activity of the spinal cord may be NSR, if the study of the sensor pad takes place at the same time as the planned surgical repair of the spinal cord, if all the following are true:

   - repair of the spinal cord would occur anyway;
- the sensor pad does not present a potential for serious risk to the health, safety, or welfare of a subject (for example, placing the pad would not prolong or interfere with the operation);
- the sensor pad is not implanted;
- the pad is not of substantial importance in diagnosing, curing, mitigating or treating disease.

VII. HOW DOES AN IRB DOCUMENT THE SR OR NSR DETERMINATION?

The IRB should write its decision in the meeting minutes. The minutes should describe the IRB’s reason for its SR or NSR determination and may also include the documentation used to establish the IDE status for the study. For an SR determination, such documentation may include, for example, a copy of the IDE approval or conditional approval letter from FDA. For an NSR determination, the documentation may include FDA’s NSR determination where the agency has made the determination. FDA will issue an NSR letter upon written request.

VIII. WHAT SHOULD AN IRB DO FOR DEVICE STUDIES THAT ARE EXEMPT FROM THE REQUIREMENTS OF THE IDE REGULATIONS (21 CFR 812.2(C))?

For studies that are exempt from the IDE regulations, the IRB does not need to decide whether the study poses a significant risk or nonsignificant risk. However, the IRB must still review the study in accordance with the IRB regulations before the investigation may begin.

IRBs should understand distinctions between certain important concepts that are frequently confused:

A. Difference between NSR and Minimal Risk Determinations

IRBs should not confuse their responsibility to make an SR/NSR determination for a device study with the concept of “minimal risk.” “Minimal Risk” is a term used in the IRB regulations in part to identify certain studies that IRBs may approve through an expedited review procedure. For a device study to be eligible for expedited review, it must be an NSR study AND present no more than minimal risk to the subject. (See 21 CFR 56.110)

B. Difference Between SR/NSR Determinations and Approval Decisions

IRBs should not confuse their responsibility to review and approve research for conduct at a clinical site with the SR/NSR determination. IRBs make the SR/NSR determination before the IRB conducts its review of the study under Part 56. The judgment about whether a study poses a significant risk or nonsignificant risk is based on the significance of the potential harm that may result from participation in the study, including the use of the device; whereas
the IRB’s decision to approve a study for implementation is based on the study’s risk-benefit assessment.

IX. WHAT ARE FDA’S RESPONSIBILITIES?

- As discussed, FDA is the final arbiter in deciding whether a device study poses a significant or nonsignificant risk. It should be noted, however, that FDA generally only sees those studies that sponsors submit to the agency or those studies for which an IRB or clinical investigator asks for FDA’s opinion.

- If FDA disagrees with an IRB’s NSR decision and determines that the study poses a significant risk, the sponsor may not begin their study until FDA approves an IDE. (See 21 CFR 812.42)

- If a sponsor submits an IDE to FDA because the sponsor presumed it to be an SR study, and FDA determines that the device study poses a nonsignificant risk, FDA will tell the sponsor in writing. The study may then be reviewed by the IRB as an NSR study.

X. EXAMPLES OF NSR AND SR DEVICES

The following examples may help sponsors and IRBs in making SR and NSR determinations. The list includes many commonly studied medical devices. Inclusion of a device in the NSR list is not a final determination because the evaluation of risk must reflect the proposed use of a device in a study.

A. Nonsignificant Risk Devices

- Caries Removal Solution
- Contact Lens Solutions intended for use directly in the eye (e.g., lubricating/rewetting solutions) using active ingredients or preservation systems with a history of prior ophthalmic/contact lens use or generally recognized as safe for ophthalmic use
- Conventional Gastroenterology and Urology Endoscopes and/or Accessories
- Conventional General Hospital Catheters (long-term percutaneous, implanted, subcutaneous and intravascular)
- Conventional Implantable Vascular Access Devices (Ports)
- Conventional Laparoscopes, Culdoscopes, and Hysteroscopes
- Daily Wear Contact Lenses and Associated Lens Care Products not intended for use directly in the eye (e.g., cleaners; disinfecting, rinsing and storage solutions)
- Dental Filling Materials, Cushions or Pads made from traditional materials and designs
- Denture Repair Kits and Realigners
- Digital Mammography
Contains Nonbinding Recommendations

- Electroencephalography (e.g., new recording and analysis methods, enhanced diagnostic capabilities, measuring depth of anesthesia if anesthetic administration is not based on device output)
- Externally Worn Monitors for Insulin Reactions
- Functional Non-Invasive Electrical Neuromuscular Stimulators
- General Biliary Catheters
- General Urological Catheters (e.g., Foley and diagnostic catheters) for short term use (< 28 days)
- Jaundice Monitors for Infants
- Low Power Lasers for treatment of pain
- Magnetic Resonance Imaging (MRI) Devices within FDA specified parameters
- Manual Image Guided Surgery
- Menstrual Pads (Cotton or Rayon, only)
- Menstrual Tampons (Cotton or Rayon, only)
- Nonimplantable Electrical Incontinence Devices
- Nonimplantable Male Reproductive Aids with no components that enter the vagina
- Ob/Gyn Diagnostic Ultrasound within FDA approved parameters
- Partial Ossicular Replacement Prosthesis (PORP)
- Total Ossicular Replacement Prosthesis (TORP)
- Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of pain (except for chest pain/angina)
- Ureteral Stents
- Urethral Occlusion Device for less than 14 days
- Wound Dressings, excluding absorbable hemostatic devices and dressings (also excluding Interactive Wound and Burn Dressings that aid or are intended to aid in the healing process)

B. Significant Risk Devices

1. General Medical Use
- Catheters for General Hospital Use - except for conventional long-term percutaneous, implanted, subcutaneous and intravascular
- Collagen Implant Material for use in ear, nose and throat, orthopedics, plastic surgery, urological and dental applications
- Surgical Lasers for use in various medical specialties
- Tissue Adhesives for use in neurosurgery, gastroenterology, ophthalmology, general and plastic surgery, and cardiology

2. Anesthesiology
- Breathing Gas Mixers
- Bronchial Tubes
• Electroanesthesia Apparatus
• Epidural and Spinal Catheters
• Epidural and Spinal Needles
• Esophageal Obturators
• Gas Machines for anesthesia or analgesia
• High Frequency Ventilators greater than 150 BPM
• Rebreathing Devices
• Respiratory Ventilators and new modes of ventilation
• Tracheal Tubes

3. Cardiovascular
• Annuloplasty Rings
• Aortic and Mitral Valvuloplasty Catheters
• Arterial Embolization Devices
• Atherectomy and Thrombectomy Catheters
• Cardiac Assist Devices: artificial hearts, ventricular assist devices, intra-aortic balloon pumps, cardiomyoplasty devices
• Cardiac Bypass Devices: oxygenators, cardiopulmonary blood pumps, axial flow pumps, closed chest devices (except Class I cardiovascular surgical instruments), heat exchangers, catheters/cannulae, tubing, arterial filters, reservoirs
• Cardiac Mapping and Ablation Catheters
• Cardiac Pacemaker/Pulse Generators: antitachycardia, esophageal, external transcutaneous, implantable
• Cardiopulmonary Resuscitation (CPR) Devices
• Cardiovascular Intravascular (vena cava) Filters
• Coronary Artery Retroperfusion Systems
• Distal Embolic Protection Devices
• Extracorporeal Counterpulsation Devices
• Extracorporeal Membrane Oxygenators (ECMO)
• Implantable Cardioverters/Defibrillators
• Intravascular Brachytherapy Devices
• Intravascular Stents
• Laser Angioplasty Catheters
• Organ Storage/Transport Units
• Pacing Leads
• Percutaneous Conduction Tissue Ablation Electrodes
• Percutaneous Transluminal Angioplasty Catheters
• Replacement Heart Valves
• Transcatheter Cardiac Occluders for atrial and ventricular septal defects, patent foramen ovale and patent ductus arteriosus
Contains Nonbinding Recommendations

- Transmyocardial Revascularization, Percutaneous Myocardial Revascularization Devices
- Ultrasonic Angioplasty Catheters
- Vascular and Arterial Graft Prostheses
- Vascular Hemostasis Devices

4. Dental
- Absorbable Materials to aid in the healing of periodontal defects and other maxillofacial applications
- Bone Morphogenic Proteins with and without bone, e.g., Hydroxyapatite (HA)
- Dental Lasers for hard tissue applications
- Endosseous Implants and associated bone filling and augmentation materials used in conjunction with the implants
- Subperiosteal Implants
- Temporomandibular Joint (TMJ) Prostheses

5. Ear, Nose And Throat
- Absorbable Gelatin Sponge
- Auditory Brainstem Implants
- Cochlear Implants
- Endolymphatic Shunt Tubes with or without valve
- ENT Cements/Adhesives
- Implantable Bone Conduction Hearing Aids
- Implantable Middle Ear Hearing Device
- Injectable Teflon Paste
- Laryngeal Implants
- Synthetic Polymer Materials
- Tissue Autofluorescent Devices
- Vocal Cord Medialization (Augmentation) Devices

6. Gastroenterology And Urology
- Anastomosis Devices
- Balloon Dilation Catheters for benign prostatic hyperplasia (BPH)
- Biliary Stents
- Components of Water Treatment Systems for Hemodialysis
- Dialysis Delivery Systems
- Electrical Stimulation Devices for sperm collection
- Embolization Devices for general urological use
- Extracorporeal Circulation Systems
- Extracorporeal Hyperthermia Systems
- Extracorporeal Photopheresis Systems
Contains Nonbinding Recommendations

- Femoral, Jugular and Subclavian Catheters
- Hemodialyzers
- Hemofilters
- Implantable Electrical Urinary Incontinence Systems
- Implantable Penile Prostheses
- Injectable Bulking Agents for incontinence
- Lithotripters (e.g., electrohydraulic extracorporeal shock-wave, laser, powered mechanical, ultrasonic)
- Mechanical/Hydraulic Urinary Incontinence Devices
- Penetrating External Penile Rigidity Devices with components that enter the vagina
- Peritoneal Dialysis Devices
- Peritoneal Shunt
- Plasmapheresis Systems
- Prostatic Hyperthermia or Thermal Ablation Devices
- Retention Type (Foley) Balloon Catheters for long term use (≥28 days)
- Suprapubic Urological Catheters and accessories
- Urethral Occlusion Devices for greater than 14 days use
- Urethral Sphincter Prostheses
- Urological Catheters with anti-microbial coatings
- Urological Stents (e.g., urethral, prostate, etc.)

7. General And Plastic Surgery
- Absorbable Adhesion Barrier Devices
- Absorbable Hemostatic Agents
- Artificial Skin and Interactive Wound and Burn Dressings
- Breast Implants
- Injectable Collagen
- Implantable Craniofacial Prostheses
- Repeat Access Devices for surgical procedures
- Sutures

8. General Hospital
- Implantable Vascular Access Devices (Ports) - if new routes of administration or new design
- Infusion Pumps (implantable and closed-loop - depending on the infused drug)

9. Neurological
- Electroconvulsive Therapy (ECT) Devices
- Hydrocephalus Shunts
- Implanted Intracerebral/Subcortical Stimulators
- Implanted Intracranial Pressure Monitors
Contains Nonbinding Recommendations

- Implanted Spinal Cord and Nerve Stimulators and Electrodes
- Neurological Catheters (e.g., cerebrovascular, occlusion balloon, etc.)
- Transcutaneous Electric Nerve Stimulation (TENS) Devices for treatment of chest pain/angina

10. Obstetrics And Gynecology
- Abdominal Decompression Chamber
- Antepartum Home Monitors for Non-Stress Tests
- Antepartum Home Uterine Activity Monitors
- Catheters for Chorionic Villus Sampling (CVS)
- Catheters Introduced into the Fallopian Tubes
- Cervical Dilation Devices
- Contraceptive Devices:
  - Cervical Caps
  - Condoms (for men) made from new materials (e.g., polyurethane)
  - Contraceptive In Vitro Diagnostics (IVDs)
  - Diaphragms
  - Female Condoms
  - Intrauterine Devices (IUDs)
  - New Electrosurgical Instruments for Tubal Coagulation
  - New Devices for Occlusion of the Vas Deferens
  - Sponges
  - Tubal Occlusion Devices (Bands or Clips)
- Cryomyolysis
- Devices to Prevent Post-op Pelvic Adhesions
- Embryoscopes and Devices intended for fetal surgery
- Endometrial Ablation Systems
- Falloposcopes and Falloposcopic Delivery Systems
- Fundal Pressure Belt (for vaginal assisted delivery)
- Gamete and Embryo Surgical Systems
- Intrapartum Fetal Monitors using new physiological markers
- New Devices to Facilitate Assisted Vaginal Delivery
- Operative Hysteroscopy and Laparoscopy
- Uterine Artery Embolization

11. Ophthalmics
- Aniridia Intraocular Lenses (IOLs) or Rings (for iris reconstruction)
- Capsular Tension Rings
- Class III Ophthalmic Lasers
Contains Nonbinding Recommendations

• Contact Lens Solutions intended for direct instillation (e.g., lubrication/rewetting solutions) in the eye using new active agents or preservatives with no history of prior ophthalmic/contact lens use or not generally recognized as safe for ophthalmic use
• Corneal Storage Media
• Extended Wear Contact Lens (i.e., including a single overnight use)
• Glaucoma Treatment Devices (e.g., trabeculoplasty devices, devices that treat ciliary bodies, devices that raise or lower intraocular pressure, aqueous shunt/drainage devices, etc.)
• Implants for Refractive Purposes (e.g., intraocular lenses, corneal implants, scleral expansion bands, etc.)
• Intraocular Lenses (IOLs)
• Keratoprostheses
• Refractive Surgical Devices (e.g., lasers, electrical current devices, thermal and non-thermal keratoplasty devices, ablation devices, expansion rings, treatment of ciliary bodies, etc.)
• Retinal Disease Treatment Devices (e.g., electrical stimulation devices to treat macular degeneration, lasers to ablate epiretinal membranes and vitreous strands, etc.)
• Retinal Prosthesis (implant)
• Retinal Reattachment Devices (e.g., fluids, gases, perfluorocarbons, perfluoropropane, silicone oil, sulfur hexafluoride, balloon catheter for retinal reattachment)
• Viscosurgical Fluids (viscoelastics)

12. Orthopedics And Restorative
• Anti-Adhesion Gels
• Bone Growth Stimulators
• Bone Morphogenetic Proteins/Biodegradable Scaffolds combination products, with or without allograft/autograft combinations and with or without metallic implant
• Bone Void Fillers (hydroxyapatite and other materials)
• Bovine Collagen Meniscus Implants
• Computer Guided Robotic Surgery
• Implantable Peripheral Neuromuscular Stimulators
• Implantable Prostheses (ligament, tendon, hip, knee, finger)
• Implantable Spinal Devices
• Injectable Sodium Hyaluronate

13. Radiology
• Boron Neutron Capture Therapy
• Hyperthermia Systems and Applicators

Also see the FDA Information Sheet Guidance on “Frequently Asked Questions about Medical Devices.”
Principles for Protecting Integrity In the Conduct and Reporting Of Clinical Trials

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Principles for Protecting Integrity in the Conduct and Reporting of Clinical Trials

Approved by AAMC Executive Committee, January 6, 2006

Issue

Public concern is high regarding the timely and complete reporting of clinical trial results, primarily when the trials are sponsored by the drug, biologics, or device industries. Because academic researchers and their institutions often play a prominent role in such trials, these concerns challenge the integrity of the academic medical research community as well as the sponsors of the trials.

Background

Despite a number of external initiatives that have heightened standards for reporting clinical trial results, the AAMC has been troubled by evidence that significant variation continues to exist within the academic community over the application of appropriate standards for analyzing and reporting the results of sponsored clinical research, especially clinical trials sponsored by industry. Accordingly, the AAMC, in collaboration with the Centers for Education and Research in Therapeutics and the BlueCrossBlueShield Association, has developed a set of principles, recommendations, and guidelines, rooted in sound science and sound ethics, to guide the medical schools, teaching hospitals, and professional societies that comprise the AAMC’s membership and be broadly disseminated in the professional community. Assuming that broad consensus is reached within academic medicine, the sponsors will work to win acceptance of the principles by industry, the FDA and NIH, non profit sponsors of clinical trials, patient advocacy groups, and ultimately, the entire medical community.

As the first step in this process, the AAMC held a small invitational conference on June 22-23, 2005. Participants were selected primarily from the academic medical community for their experience in clinical research and research ethics, with special focus on expertise in the area of industry sponsored clinical trials. The charge to the conferees was to articulate a set of principles for academic medicine that should guide institutions and their researchers in the ethical and operational aspects of data access, analysis, and reporting of clinical research studies and would thereby help to assure integrity and credibility in the conduct and reporting of clinical trials. The conferees agreed to avoid what are routinely considered business or legal issues associated with clinical trials contracting (e.g., intellectual property, indemnification, and the like) and focused instead on study participation, access to data and analysis among investigators, reporting of results and publication, data sharing following publication, and trial registration.

The principles developed at the conference were endorsed by the AAMC’s governance in September 2005 and shared widely with medical, scientific, and patient organizations, the FDA and NIH, non profit sponsors of clinical trials, patient advocacy groups, and senior biopharmaceutical executives, to identify areas of agreement and concern among those diverse stakeholders in clinical research. In response to comments, the document was revised to resolve ambiguous language and clarify certain technical
requirements. The revised principles were approved by the AAMC Executive Committee on January 6, 2006.

**Consensus Principles**

The following principles should apply to all clinical trials conducted in academic medical institutions regardless of the source of funding. They encompass single site as well as multisite studies, although operationalization of the principles may differ across study types and sizes. For purposes of these principles, “clinical trials” should be defined by reference to the ICMJE definition: “Any research project that prospectively assigns human subjects to intervention and comparison groups to study the cause-and-effect relationship between a medical intervention and a health outcome.” “Medical intervention” means “any intervention used to modify a health outcome”, including “drugs, surgical procedures, devices, behavioral treatments, process-of-care changes, and the like.”¹ This definition explicitly excludes phase 1 and early phase 2 studies (but not all late phase 2 studies), and it includes all phase 3 and 4 clinical trials, including studies of new indications for approved products.

**Publications and Public Availability of Research Results**

1. Researchers and their institutions have an ethical obligation when conducting human research to seek to make the results available publicly.

2. Contracts between sponsors and institutions for conducting clinical trials should require a good faith effort to publish the results of such trials in a peer reviewed journals in a timely fashion.

3. Contracts for clinical trials should contain a commitment of adequate funding to cover the full costs of the analysis defined in the protocol and the costs associated with publishing the results. This principle applies even when the study is terminated for any reason prior to meeting its pre-specified objectives.

4. All trials meeting the ICMJE requirements² for registration should make their results publicly available, by means of a link to any peer reviewed publications and by posting the results in an online accessible repository, within 18 months of submission of a manuscript for publication.

5. After publication of the results, the sponsor, the investigators, and their institutions should adopt a model for public sharing of the data underlying publications similar to that of NIH,³ which permits exceptions for confidential or proprietary information.


² Ibid. The World Health Organization is leading an international effort to promote registration of clinical trials, but has not yet gained consensus on the issue of “masking” of certain elements in the minimum data set required for registration. Because of continuing uncertainty, the WHO effort is acknowledged but not included as an alternative to the ICMJE registration requirements.

Registration of Clinical Trials

6. Within 21 days of initiating enrollment of participants, any clinical trial covered by these principles should be fully registered pursuant to the ICMJE requirements\textsuperscript{4} for registration. Registration must include the assignment of a unique identifying number to each clinical trial.

7. Registration should be accomplished either in clinicaltrials.gov or in another public, non-profit, international registry and should include all the elements required by that registry.

8. Insofar as is feasible, trial registration data should be regularly updated to include a link to all published reports associated with the study.

Lead Investigator and Steering Committee

9. A multisite clinical trial, at the outset, should identify a lead or principal investigator and a steering committee to represent the full body of investigators.

Publication and Analysis Committee

10. A multisite clinical trial, at the outset, should establish a publication and analysis committee [hereinafter P&A committee]. It is essential that the P&A committee be independent of the sponsor’s control, have access to the full data set, understand and implement the prespecified analysis plan, and have the resources and skills both to interpret that analysis and perform additional analysis if required. In order to prevent any appearance of undue influence by the sponsor, the P&A committee should contain a majority of participating, non-sponsor-employed investigators, with appropriate skills in analysis and interpretation of clinical trials. The P&A committee and the steering committee may have the same membership.

11. The P&A committee in multisite clinical trials (or the principal investigator of single site studies), through a qualified expert of its choosing, preferably a member of that committee, should have the right to access any data generated during the study that the committee deems necessary to ensure the integrity and validity of the study and its full reporting.

12. The P&A committee in multisite clinical trials (or the principal investigator in single site studies) should require that the sponsor of the study perform its analysis of trial data in a defined period of time. The committee (or PI) should be able to conduct its own analysis through an expert selected by it, to the extent it deems this necessary. Whenever feasible, the expert should be agreed upon by the P&A committee and the sponsor.

13. The sponsor should share with the P&A committee all analyses called for by the study that the sponsor conducts of any biological materials it receives during the course of the study.

\textsuperscript{4}See note 1.
14. The P&A committee or PI should make a good faith effort to disseminate the results of the study through peer reviewed mechanisms.

Individual Publication

15. Site-specific publications in multisite trials have an unavoidable potential for bias. Because they are almost never part of the original analytic plan, they are often misleading, and should be strongly discouraged. However, to respect an academic institution’s commitment to academic freedom, site-specific analyses should nonetheless be permitted with conditions. Accordingly, an individual site investigator in a multisite trial should be free to analyze and publish data from the individual site, consistent with sound principles of science and analysis, but only after review and comment by the P&A committee and only after publication of the study as a whole, or, in the absence of acceptance of the full publication, within 2 years from the specified end points or earlier termination of the study.

Authorship

16. Ghost or guest authorship is unacceptable. Authorship implies independent, substantial, and fully disclosed participation in the study and in the preparation of the manuscript. It is acceptable for employees of the sponsor to participate in drafting and publication activity, but only if their roles are fully disclosed.

17. Institutions conducting clinical trials should adopt as policy the standards of authorship defined by the ICMJE.

18. Where applicable, investigators should use the CONSORT principles\(^5\) as guidance for publication of trial results.

19. Investigators should fully disclose, and journals should publish, the existence of all relevant financial interests, including consultancies of any investigator, in all communications of trial results.

20. Any manuscript submitted for publication should accurately disclose the role of each author in conducting the study and preparing the manuscript. Such information should also be disclosed in any public presentation of study results, to the extent practicable.

21. Manuscripts submitted for publication should disclose all previous publications involving the same protocol or database.

22. Manuscripts submitted for publication should be accompanied by the protocol and pre-specified analysis plan and all dated amendments to them, and any deviations to the pre-specified plan should be identified and discussed.

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