The Wright Center for Graduate Medical Education (WCGME)

Institutional Review Board (IRB)

(WCGME-IRB)

Investigator's Guide

Reviewed	February 1999
Revised	January 2002
Revised	July 2006
Reviewed	October 2006
Revised	January 2011
Reviewed	November 2013

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1. Name, Sponsor, Location:

A. **Name**: The name of this board shall be the Wright Center for Graduate Medical Education Institutional Review Board (WCGME-IRB).

B. **Sponsor:** This board, sponsored by the Wright Center for Graduate Medical Education, shall serve The Wright Center for Graduate Medical Education, The Wright Center Medical Group, PC and shall be available, upon request, to other area institutions.

C. **Location:** The location of the WCGME-IRB shall be:

WCGME-IRB Administrative Offices
501 Madison Avenue
Scranton, PA 18510
Phone: (570) 343-2383 x2261
FAX (570) 207-4025
Email: wcgme-irb@thewrightcenter.org

D. **Purpose:** The local IRB is established in accordance with Food and Drug Administration (FDA) regulations (Requirements of 21 CFR 50 and 56). The purpose of the board is to review biomedical and behavioral research involving human subjects/patients in order to protect the rights of the human subjects/patients of such research.

In reviewing research that involves human subjects, the Institutional Review Board's function shall be to make certain that:

- The rights and welfare of any human subjects/patients will be adequately protected.
- Legally effective informed consent will be obtained by adequate and appropriate methods in accordance with the provisions of applicable Federal regulations.
- The risks to the subjects/patients are so outweighed by the potential benefits to the subjects/patients and the importance of the knowledge to be gained as to warrant a decision to allow the subject/patient to accept these risks.
- The conduct of the research activities will be reviewed at timely intervals.

2. Jurisdiction:

The Institutional Review Board's jurisdiction shall be defined as follows:

The IRB will make itself available to the participating institutions as defined above, to review all research activity within the institutions in which human beings may be at risk. Research protocols proposed for implementation will be reviewed regardless of

the source of support for the research activity. Research activity carried on in whole or in part on the premises of The Wright Center for Graduate Medical Education, The Wright Center Medical Group, PC or the locations of organizations who have a current Federal Wide Assurance (FWA) and IRB Authorized Agreement with The Wright Center for Graduate Medical Education Institutional Review Boar, will be subject to review by the WCGME-IRB.

3. Membership:

The following membership criteria will serve as a framework for Institutional Review Board representation.

A. The WCGME-IRB shall have at least five members with varying backgrounds to promote complete and adequate review of local clinical investigations.

B. The WCGME-IRB shall not be represented by members of one profession or consist entirely of men or women.

C. The WCGME-IRB shall include at least one member whose primary concerns are in non-scientific areas, e.g., lawyers, clergy, and ethicists.

D. The WCGME-IRB shall include one member who is not otherwise affiliated with the institutions represented.

E. The WCGME-IRB may invite, at its discretion, individuals with competence in special areas to assist in the review of complex issues which require expertise beyond or in addition to that available on the IRB. These individuals may not vote with the IRB.

F. No WCGME-IRB member may participate in the review of any project in which the member has a conflicting interest, except to provide information requested by the IRB.

G. Ex-officio members nominated by organizations having a special relationship with the WCGME-IRB, must be approved by action of the WCGME-IRB general (Those members having a vote.) membership. Ex-officio members will serve as the representative of the nominating organization to provide a communication channel between both organizations. Ex-officio members may participate in discussions but may not vote, make or second motions and are not included as part of the general membership of the WCGME-IRB and as such will not count toward quorum requirements as set forth in these By-Laws.

4. Current Members:

A list of the current members of the WCGME-IRB is posted on the WCGME-IRB web page at http://thewrightcenter.org. Follow the link to the WCGME-IRB page and select the “Members” link.

5. Meetings:

A. The WCGME-Institutional Review Board meetings will be scheduled on the fourth Thursday of the month at 8:00 A.M. Currently meetings are held in the Second

Floor Small Meeting Room of the McGowan Conference Center, Regional Hospital of Scranton, Scranton, PA.

B. The Board may elect not to meet during certain months.

C. All notifications regarding meetings will be sent out at least one week prior to the scheduled meeting.

D. Additional meetings, as needed, may be scheduled between regular sessions to meet emergencies or other unforeseen circumstances.

6. WCGME-IRB Fee Schedule:

A fee is charged to cover the administrative operating expenses of the board. Fees are charged for the review of industry-sponsored, government-sponsored and other grant funded research protocols. This policy applies to the initial and continuing review of protocols. Fees for continuing (i.e., renewal) review will be charged on an annual basis, regardless of the duration of the approval period. Fees may be adjusted periodically as necessary. The current fee schedule is posted annually on the WCGME-IRB web page at http://www.strpweb.org. The WCGME-IRB web page is an important source of information for investigators and should be referred to prior to submitting any protocol to the board for review.

The principal investigator submitting the protocol for review is responsible for the timely payment of all fees charged for IRB reviews.
Reductions in IRB review fees will be considered based upon documented budget limitations. Requests must be submitted in writing to the WCGME-IRB Administrator along with all appropriate substantiating documentation. The submitting principal investigator will be notified via a memo whether or not the request has been granted. Requests will be reviewed on a case by case basis.

7. Protocol Review Process:

A. Review Criteria:

All investigational activities in which human subjects may be at risk require review and approval by the Institutional Review Board. An individual is considered to be at risk if exposed to the possibility of harm -- physical, psychological, social, legal or other -- as a consequence of participation as a subject in any activity which departs from the application of the established and accepted methods required to meet his/her medical needs. Copies of the by-laws will be available to all organizations holding a current FWA and IRB Authorization Agreement with the Wright Center for Graduate Medical Education Institutional Review Board.

B. Review Process:

- The Principal Investigator shall submit a signed WCGME-IRB Protocol Submission Form for each protocol submission.

- Protocols, consent form and all other necessary documentation will be sent to the IRB Administrative Office by the required submission date. Submission dates for regularly scheduled meetings of the WCGME-IRB are posted on the WCGME-IRB web page located at: http://www.thewrightcenter.org.
- The WCGME-IRB Protocol Submission Form requires that the Principal Investigator sign in two locations. The protocol will not be processed for review unless the required signatures are affixed at the time submitted.
- If necessary, WCGME-IRB members and/or others with special pertinent expertise shall be identified by the IRB chairman or Co-Chairman for review process.
- The protocol will be listed as an agenda item for IRB meeting.
- The Protocol Submission Form, protocol, consent form, and other appropriate documentation will be provided to the primary and secondary WCGME-IRB reviewers in printed form.
- The Protocol Submission Form, protocol, consent form and other appropriate documentation will be made available to all board members not assigned as primary or secondary review by up-loading the documentation in PDF format to the WCGME-IRB web page.
- A Primary and Secondary Protocol Reviewer will be assigned to the protocol by the IRB Chairman or designate.
- At the scheduled meeting, the Principal Investigator will present a summary review of the protocol for the board members.
- The Primary and Secondary reviewers will comment on the protocol and patient informed consent document and make their recommendation regarding the approval of the protocol.
- The Primary and Secondary reviewers are required to complete the “Checklist for Review of Proposals” and submit it to the WCGME-IRB Administrator at the end of the meeting.
- All WCGME-IRB Board members will also be given an opportunity to comment on the protocol and documentation.
- All WCGME-IRB Board members may complete the “Checklist for Review of Proposals” and submit it to the WCGME-IRB Administrator at the end of the meeting for inclusion in the meeting records.
- After hearing all discussion, a vote by WCGME-IRB members will be taken. A decision will be made to accept, require modifications or reject the protocol. In some cases a decision may be deferred (tabled) pending additional information from the Principal Investigator. (In no case will a decision on a protocol be tabled longer then the next scheduled meeting of the WCGME-IRB.)

- The decision will be given to the Principal Investigator, promptly in writing (generally with 2-5 working days after the meeting), of the outcome of the IRB review including any particular requirements.

C. Expedited Review:

- The Secretary, HHS, has established, and published as a Notice in the FEDERAL REGISTER, a list of categories of research that may be reviewed by the IRB through an expedited review procedure.
- An IRB may use the expedited review procedure to review either or both of the following:
  - some or all of the research appearing on the list and found by the reviewer(s) to involve no more than minimal risk,
  - Minor changes in previously approved research during the period (of one year or less) for which approval is authorized. Under an expedited review procedure, the review may be carried out by the IRB chairperson or by one or more experienced reviewers designated by the chairperson from among members of the IRB. In reviewing the research, the reviewers may exercise all of the authorities of the IRB except that the reviewers may not disapprove the research. A research activity may be disapproved only after review in accordance with the non-expedited procedure set forth in §46.108(b).
  - Each IRB which uses an expedited review procedure shall adopt a method for keeping all members advised of research proposals which have been approved under the procedure. The WCGME-IRB will report all expedited reviews to the full membership at the next regular meeting of the board. Members not present at that meeting will receive notification via the published minutes of the meeting.

8. Voting:

Requirements for a quorum necessary to conduct business shall be:

A. A majority (51% or greater) of the voting members must be present, including at least one voting member whose primary professional qualification is in non-scientific areas.

B. In order for the research to be approved, the protocol must receive a favorable vote of a majority (51% or greater) of those voting members present at the meeting. An IRB Member presenting a protocol for review will not participate in the vote nor will they be counted as a voting member to attain the required 51% as required above.

C. The Principal Investigator and all persons directly involved with the protocol will leave the room while the vote is taken. The non-presence and non-participation in voting shall be recorded in the Institutional Review Board minutes. The vote shall be indicated by a show of hands.

9. Voting Outcome:

The review of each protocol shall culminate in one of four (4) categories:

A. Approval: This means no further action is necessary and the investigator may proceed with the research.

B. Conditional Approval: This means that the Institutional Review Board has identified certain problems in either the protocol or the consent form. Following notification to the investigator, these protocols are revised and returned for review by the Chairman or Co-Chairman. The Institutional Review Board may authorize the Chairman or Co-Chairman, or other member to review the Principal Investigator's response and the Institutional Review Board's suggested revision and to issue final approval for the research protocol. The Institutional Review Board will authorize such executive approval on a case-by-case basis. If the specified conditions are met, a certification of approval shall be issued without further consideration by a full committee. Committee members should have access to the revised materials at the next scheduled meeting. A record of these executive actions should be included in the Institutional Review Board minutes.

C. Deferred: This means tabling a protocol in order to obtain clarification, e.g., to request an outside opinion.

D. Disapproval: This means the Institutional Review Board does not approve the protocol. If the Institutional Review Board decides to refuse a research activity, it shall include in written notification the statement of reasons for the decision and give the investigator an opportunity to respond in writing.

E. IRB members will vote “yes”, “no’, or “abstain”. These votes will be recorded in the IRB meeting minutes.

10. Criteria for Institutional Review Board approval of Research:

In order to approve research the Institutional Review Board shall determine that all of the following requirements are satisfied:

A. Procedures which are consistent with sound research design and do not unnecessarily expose subjects to risk are used.

B. Risks to subjects are acceptable in relation to anticipated benefits. In evaluating risks and benefits, the Institutional Review Board shall consider only those risks and benefits that may result from the research.

C. Selection of subjects is equitable. In making this assessment the Institutional Review Board shall take into account the purposes of the research and the setting in which the research will be conducted.

D. Informed consent will be obtained from each prospective subject or the subject's legally authorized representative.

E. Informed consent will be appropriately documented and comply with all relevant Federal Regulations.

F. When appropriate, the research plan shall make adequate provisions for monitoring the data collected to insure the safety of subjects.

G. When appropriate, there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of the data.

IRB Review Procedures for Medical Device Research:

H. Definitions

1. Investigational Medical Device means any instrument, apparatus, or other similar or related article, including component, part, or accessory, that is the object of a clinical trial and that has not yet received marketing approval by the FDA for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment, or prevention of disease, in man or other animals, or intended to affect the structure of any function of the body of man or other animals.

2. Investigational Use of Marketed Products means the investigational use of an approved marketed device or other health product with the principal intent of developing information about the safety and efficacy of the device or other health product for uses other than those for which it was approved by the FDA. The investigational use of marketed products requires an IDE and approval of the clinical trial by the IRB.

3. 510(k) Device means a medical device that is determined by the FDA to be substantially equivalent to a device that was or is being legally marketed (i.e., predicate device) and will grant FDA approval status typically after a 90 day review. The sponsor or company will provide this verification to the investigator in writing for IRB submission. A procedure that will involve a device with a 510(k) classification will require IRB full-review if not used as part of the practice of medicine only.

4. IDE Number is a number assigned to an Investigational Medical Device approved by the FDA for use in a clinical trial involving human subjects.

5. "Significant Risk Device" means an Investigational Medical Device that presents a potential for serious risk to the health, safety, or welfare of the human subject. The study must have both FDA approval (IDE) and IRB approval for the investigation to begin. A Significant Risk Device is:

    a. intended for use as an implant and presents a potential for serious risk to the health, safety, or welfare of the patient; or

    b. purported or represented to be of use in supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of the patient; or

    c. Intended for a use that is 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 the patient.

6. "Non-significant Devices" are subject to the abbreviated requirement which involves approval process differences. If the IRB approves an investigation as a nonsignificant risk, the investigation is considered to have an IDE under the abbreviated FDA requirements and the investigation can begin immediately following institutional research approval.

I. Determination of Device Risk by the Sponsor or Manufacturer

1. All clinical trials involving Investigational Medical Devices should include a written determination (i.e., protocol, memorandum, and brochure) by the Sponsor of whether the Investigational Medical Device poses a "Significant Risk" or a "Non-significant Risk".

2. If the Sponsor has determined that the Medical Device presents a "Significant Risk", the PI must provide the IRB with evidence that the Investigational Medical Device has received an IDE from the FDA.

J. IRB Review Procedures for Medical Device Research

1. Medical Devices will be independently reviewed by the full-board IRB according to the standard format of the WCGME-IRB and will receive a determination by the IRB of "Significant Risk" or "Non-significant Risk". The IRB will review this information and may or may not agree with the Sponsor's determination. The IRB may consult the FDA for its opinion on the risks associated with the Investigational Medical Device.

2. In general, full-board IRB review is required for both "Significant" and "Non-significant Risk" devices. They may also be considered minimal risk studies, and thus may be reviewed through the expedited review procedure established by the IRB.

3. In addition, if the Investigational Medical Device is a "Significant Risk" Device or if the IRB disagrees with the Sponsor's determination that the Investigational Medical Device presents "Non-significant Risk" to human subjects, the Sponsor and/or the WCGME- IRB will be required to notify the FDA that a "Significant Risk" determination was made by the IRB.

11. Informed consent:

The basic elements of the informed consent, as defined in Section 50.25 of 21 CFR Part 50 of the Federal Regulations include:

A. A statement that the study involves research, an explanation of the purpose of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental.

B. A description of any reasonably foreseeable risks or discomforts to the subject.

C. A description of any benefits to the subject or to others which may reasonably be expected from the research.

D. A disclosure of appropriate alternative procedures or course of treatment, if any, that might be advantageous to the subject.

E. 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, the sponsor of the protocol, and any other parties authorized by law, may inspect the records.

F. 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.

G. An explanation of whom to contact for answers to pertinent questions about the research and research subject's rights, and whom to contact in the event of a research-related injury to the subject.

H. 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.

I. Additional elements of informed consent. When appropriate, one or more of the following elements of information must be provided to each subject:
    a. A statement that a 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.
    b. Anticipated circumstances under which the subject’s participation may be terminated by the investigator without regard to the subject’s consent.
    c. Any additional costs to the subject that may result from participation in the research.
    d. The consequences of a subject’s decision to withdraw from the research and procedures for orderly termination of participation by the subject.
    e. A statement that significant new findings developed during the course of the research which may relate to the subject’s willingness to continue participation will be provided to the subject.
    f. The approximate number of subject’s involved in the study.

12. Hospital Review:

Research that has been approved by the WCGME-Institutional Review Board may be subject to further review and may be disapproved by officials of IRB Member Institutions, or other hospitals seeking Institutional Review Board review of research activity. However, organizations holding a Federal Wide Assurance (FWA) with the WCGME-IRB may not approve research if it has been disapproved by the WCGME-IRB.

13. Reporting Unanticipated Risks, Misconduct and Non-compliance:

The Investigator is responsible for reporting unanticipated problems or adverse events to the WCGME-IRB Chairperson and the WCGME-IRB Administrator.

Any instance of serious or continuing non-compliance with WCGME-IRB policies and procedures or the requirements or determinations of the WCGME-IRB will be reported in the same manner.

14. Suspension or Termination of Institutional Review Board Approval of Research:

A. The Institutional Review Board shall have the authority to suspend or terminate approval of research that:
   - Is not being conducted in accordance with the Institutional Review Board requirements.
   - Has been associated with unexpected serious harm to subjects.
   - Has failed to comply with the conditions of review as set forth by the WCGME-IRB.

B. Any suspension or termination of approval shall include a statement in writing of the reasons for the Institutional Review Board's action and shall be reported promptly to the investigator, appropriate institutional officials and to the FDA.

15. Instructions for Documentation Preparation:

A. Full Board/New Protocol Review:
   - The Principal Investigator shall submit a signed WCGME-IRB Protocol Submission Form for each protocol submitted.
   - The protocol, consent form and all other necessary documentation will be sent to the IRB Administrative Office by the required submission date. (Submission dates for regularly scheduled meetings of the WCGME-IRB are posted on the WCGME-IRB web page.)
   - The documentation for review will normally include:
     . The research protocol with amendments, if any (One hard copy and one electronic copy in “pdf” format).
     . The Informed Consent document(s) (One hard copy and one electronic copy in “pdf” format).
     . Resume(s) of clinical investigator(s) and sub-investigator(s) (One hard copy and one electronic copy in “pdf” format).
     . Advertising copy for subject/patient solicitation (One hard copy and one electronic copy in “pdf” format).

. Any other appropriate material which can help the WCGME-IRB in its understanding of the research proposal (One hard copy and one electronic copy in “pdf” format).

Please note: Incomplete documentation will result in a delay reviewing the protocol.

The documentation may be mailed to:

The Wright Center for Graduate Medical Education-Institutional Review Board
501 Madison Avenue
Scranton, PA 18510

- The WCGME-IRB Protocol Submission Form requires that the Principal Investigator sign in two locations (One hard copy and one electronic copy in “pdf” format). The protocol will not be processed for review unless the required signatures are affixed at the time submitted.

B. Expedited Review:

- For studies of minimal risk, an expedited review may be requested. This review can occur during any business day of the week. (Approved research protocols that have achieved no accrual within the previous year will receive expedited review until such time as patient(s) have been accrued. At that time, the protocol will require full/continuing review by the WCGME-IRB.)
- The Principal Investigator shall submit a signed WCGME-IRB Protocol Submission Form for each protocol submitted.
- The documentation for review is the same as a Full Board/New Protocol Review listed on page 3, except only one (1) copy of the protocol and advertising and three (3) copies of the consent form need to be submitted,

Appendix A: Protocol Review Guidelines

General Information for the Reviewer:

GOAL - To produce a **final** protocol that will provide a feasible, consistent and safe method of treatment administration.

RATIONALE - The purpose of this review is to:

1. Assess the ability to implement the treatment plan as described.
2. Provide consistency of drug information between all sections of the protocol.
3. Provide for safe administration of all chemotherapy, by insuring that protocols are written in a manner to reduce the risk of potential errors.
4. Minimize the cost of therapy by recommending more efficient methods of administration.

OBJECTIVES

1. The reviewer should read the entire protocol, placing the major focus on the Treatment Plan Section. Reviewer should target inconsistencies within the protocol that would improve implementation of the treatment plan; Emphasis should also be placed on drug information, drug procurement, pharmacist blinding issues, roadmaps, critical pathways, appendices and consent form.

2. After problem identification, solutions should be developed and specific suggestions made. E.g. if the dosing of an oral medication needs to have dose-rounding guidelines, then not only suggest that such guidelines need to be developed and included, but provide an example of specific guidelines that would be useful.

3. Reviewer must provide written review with suggestions and concerns. The reviewer should note the section or page referred to for the author to refer back to.

4. Two reviewers will be assigned to review the protocol, a primary and secondary person. Reviewer should make every attempt to meet deadlines for review.

Review Guidelines:
This checklist must be completed by the primary and secondary reviewer. It is to be given to the WCGME-IRB Administrator at the conclusion of the meeting and will be filed with the protocol reviewed. (All members of the board are encouraged to complete and submit this checklist for each protocol.)

CHECKLIST USED BY WCGME-IRB FOR REVIEW OF PROPOSALS (revised January 2006)

Regulatory review requirement:	Reviewer input:		
1. The proposed research design is scientifically sound & will not unnecessarily expose subjects to risk.	Yes	No	N/A
a. Is the hypothesis clear? Is it clearly stated?			
b. Is the study design appropriate to prove the hypothesis?			
c. Will the research contribute to generalizable knowledge and is it worth exposing subjects to risk?			
2. Risks to subjects are *reasonable* in relation to anticipated benefits, if any, to subjects, *and* the importance of knowledge that may reasonably be expected to result.	Yes	No	N/A
a. Does the IRB consider the level of risk to be greater than minimal?			
b. Does the PI consider the level of risk/discomfort/ inconvenience to be greater than minimal?			
c. Is there prospect of direct benefit to subjects?			
3. Subject selection is equitable.	Yes	No	N/A
a. Based upon who is to be enrolled (Men? Women? Ethnic minorities? Children (rationale for inclusion/exclusion addressed)? Seriously-ill persons? Healthy volunteers?) is the subject selection equitable?			
b. Are these subjects appropriate for the protocol?			
4. Additional safeguards required for subjects likely to be vulnerable to coercion or undue influence.	Yes	No	N/A
a. Are appropriate protections in place for vulnerable subjects, e.g., pregnant women, fetuses, socially- or economically-disadvantaged, decisionally-impaired?			
5. Informed consent is obtained from research subjects or their legally authorized representative(s).	Yes	No	N/A
a. Does the informed consent document include the eight required elements?			

b. Is the consent document understandable to subjects?			
c. Is the following information listed appropriately in the consent? The person who will obtain informed consent (PI, nurse, other?) and in what setting?			
d. If appropriate, is there a children's assent?			
e. Is the IRB requested to waive or alter any informed consent requirement?			
6. Risks to subjects are minimized.	Yes	No	N/A
a. Does the research design minimize risks to subjects?			
b. Would use of a data & safety monitoring board or other research oversight process enhance subject safety?			
7. Subject privacy & confidentiality are maximized.	Yes	No	N/A
a. Will personally-identifiable research data be protected to the extent possible from access or use?			
b. Are any special privacy & confidentiality issues properly addressed, e.g., use of genetic information?			

Reviewer's Signature: _____ Date: _____

Reviewer's Name: _____
(Printed or typed)

Place any additional comments below. Us an additional sheet of paper if necessary.

APPENDIX B: Human Subject Regulations Decision Charts:

September 24, 2004

The Office for Human Research Protections (OHRP) provides the following graphic aids as a guide for institutional review boards (IRBs), investigators, and others who decide if an activity is research involving human subjects that must be reviewed by an IRB under the requirements of the U.S. Department of Health and Human Services (HHS) regulations at 45 CFR part 46. OHRP welcomes comment on these decision charts. The charts address decisions on the following:

- whether an activity **is research** that must be reviewed by an IRB
- whether the review may be performed by **expedited procedures**, and
- whether **informed consent** or its documentation may be waived.

Considerations

The charts are intended to assist IRBs, institutions, and investigators in their decision-making process and should not be used as substitutes for consulting the regulations. OHRP cautions that the full text of applicable regulatory provisions should be considered in making final decisions.

These charts are necessarily generalizations and may not be specific enough for particular situations. Other guidance documents are available related to specific topics, at OHRP Policy Guidance by Topic (http://www.hhs.gov/ohrp/policy/index.html#topics). OHRP invites inquiries for additional information.

The charts do not address requirements that may be imposed by other organizations, such as the Food and Drug Administration, National Institutes of Health, other sponsors, or state or local governments.

Chart 1: Is an Activity Research Involving Human Subjects?

Chart 2: Is the Human Subjects Research Eligible for Exemption?

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

Chart 4: Does exemption 45 CFR 46.101(b)(2) or (b)(3) (for Tests, Surveys, Interviews, Public Behavior Observation) Apply?

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

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

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

Chart 8: May the IRB Review Be Done by Expedited Procedures?

Chart 9: May the IRB Continuing Review Be Done by Expedited Procedures?

Chart 10: May Informed Consent Be Waived or Consent Elements Be Altered under 45 CFR 46.116(d)?

Chart 11: May Documentation of Informed Consent Be Waived Under 45 CFR 46.117(c)?

Chart 1: Is an Activity Research Involving Human Subjects Covered by 45 CFR part 46?

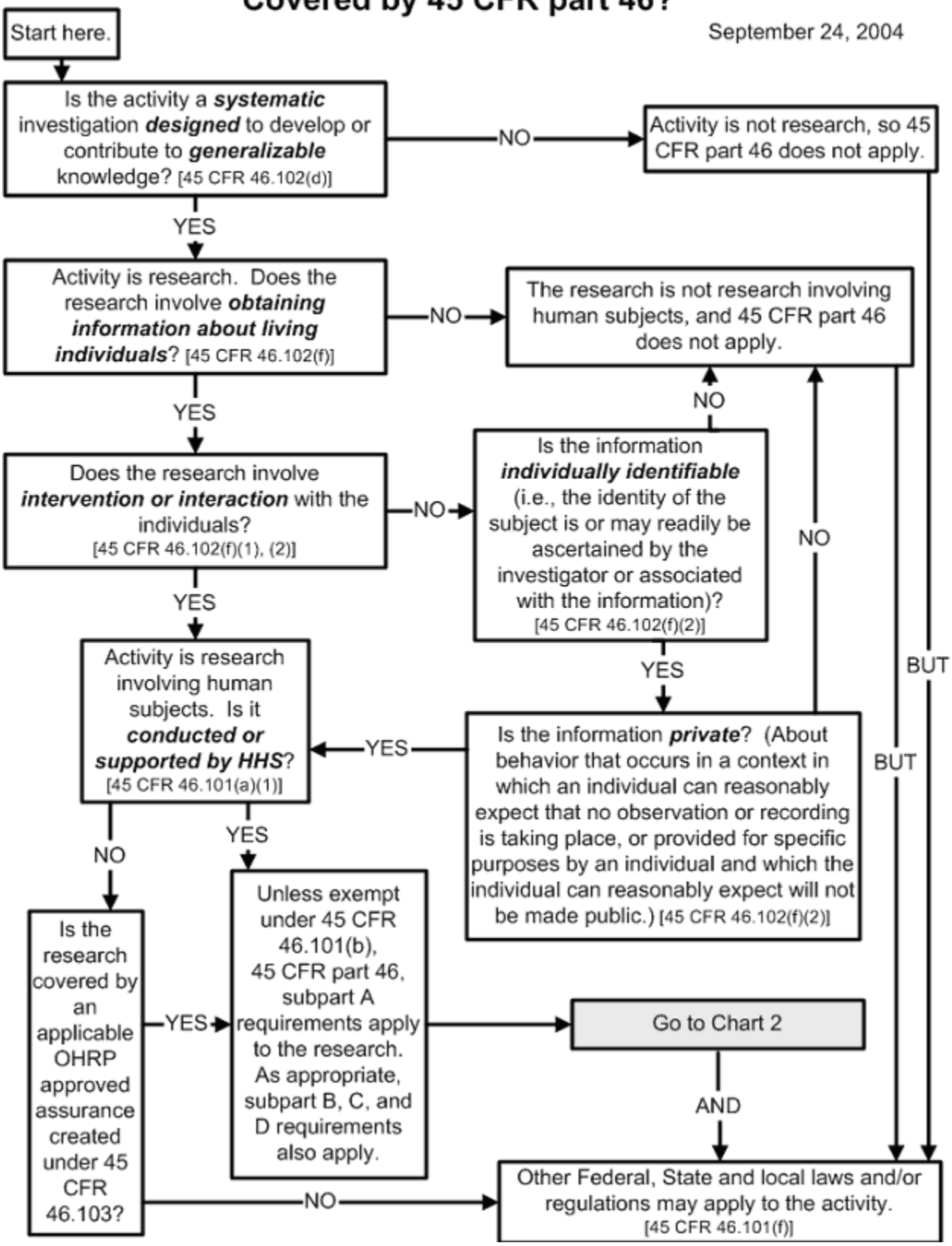


Chart 2: Is the Research Involving Human Subjects Eligible for Exemption Under 45 CFR 46.101(b)?

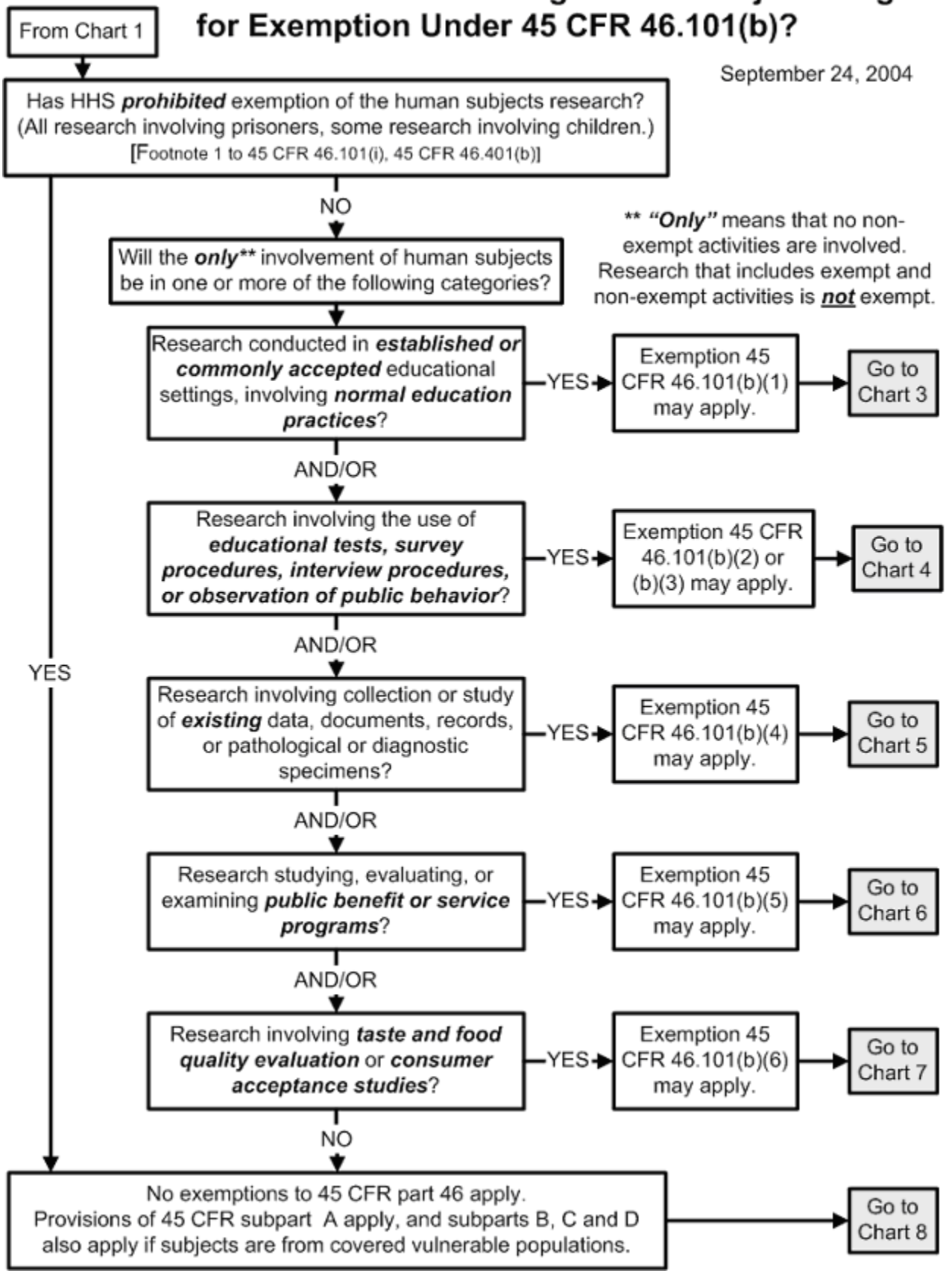
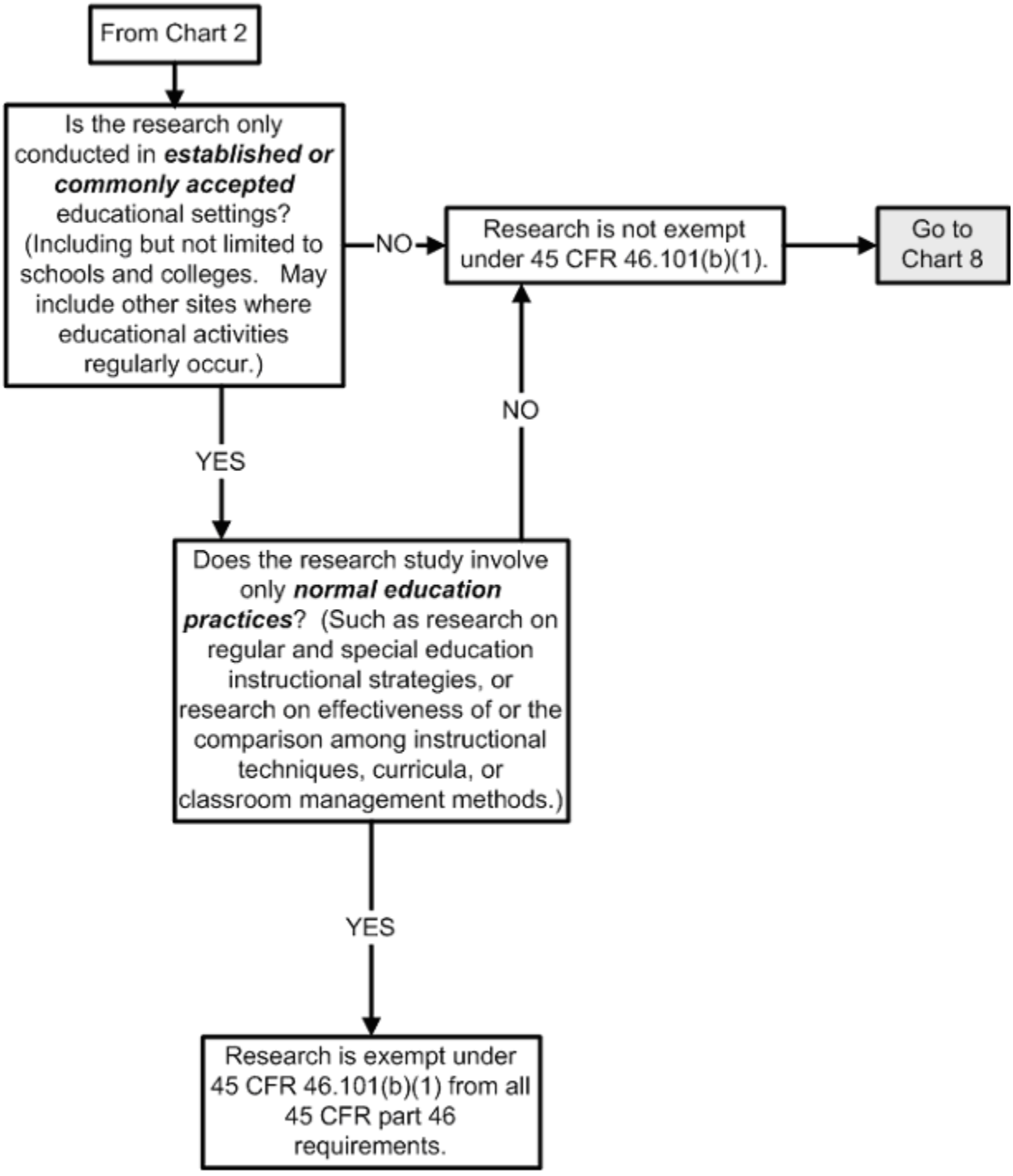
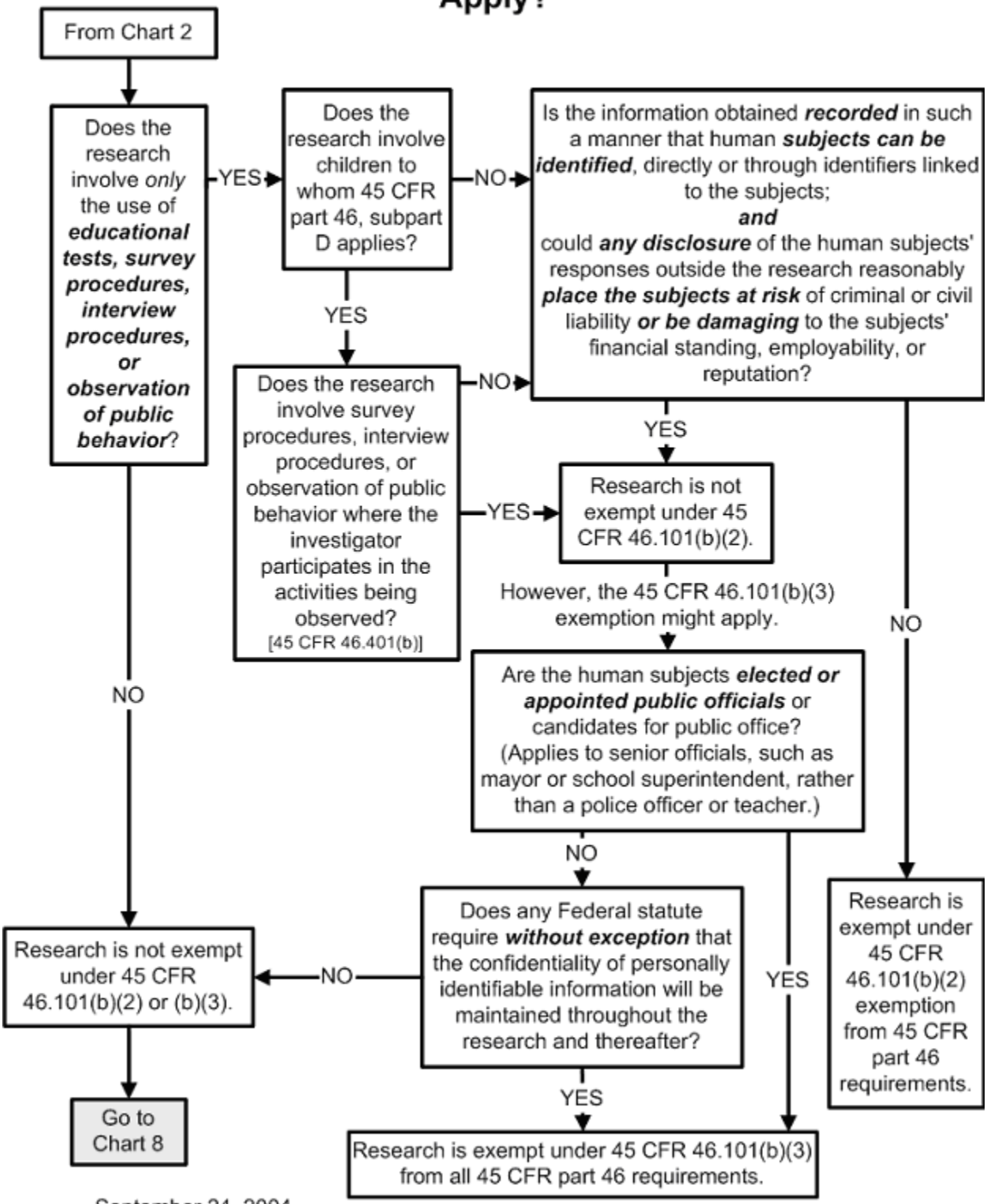


Chart 3: Does Exemption 45 CFR 46.101(b)(1) (for Educational Settings) Apply?



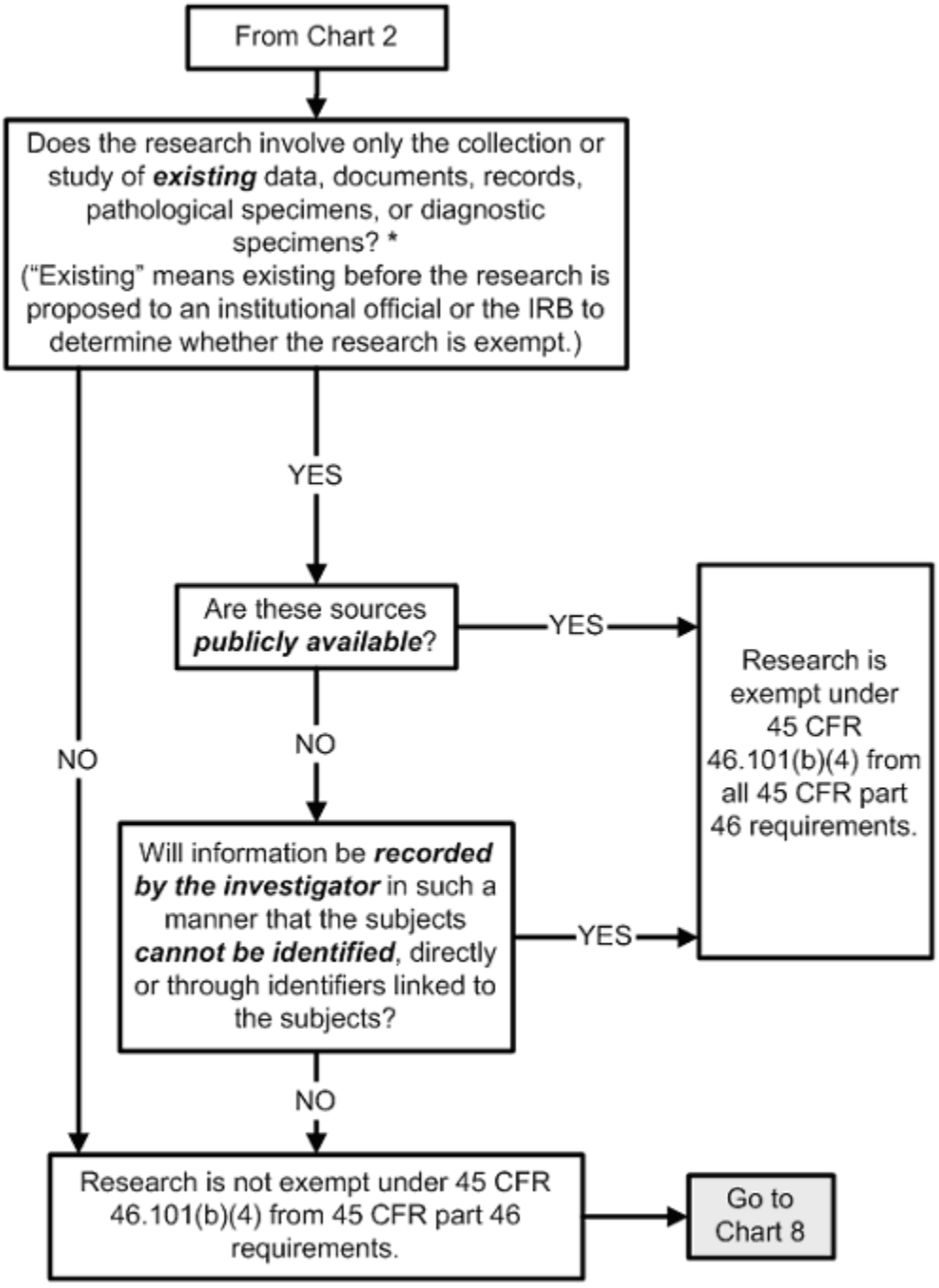
September 24, 2004

Chart 4: Does Exemption 45 CFR 46.101(b)(2) or (b)(3) (for Tests, Surveys, Interviews, Public Behavior Observation) Apply?



September 24, 2004

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



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

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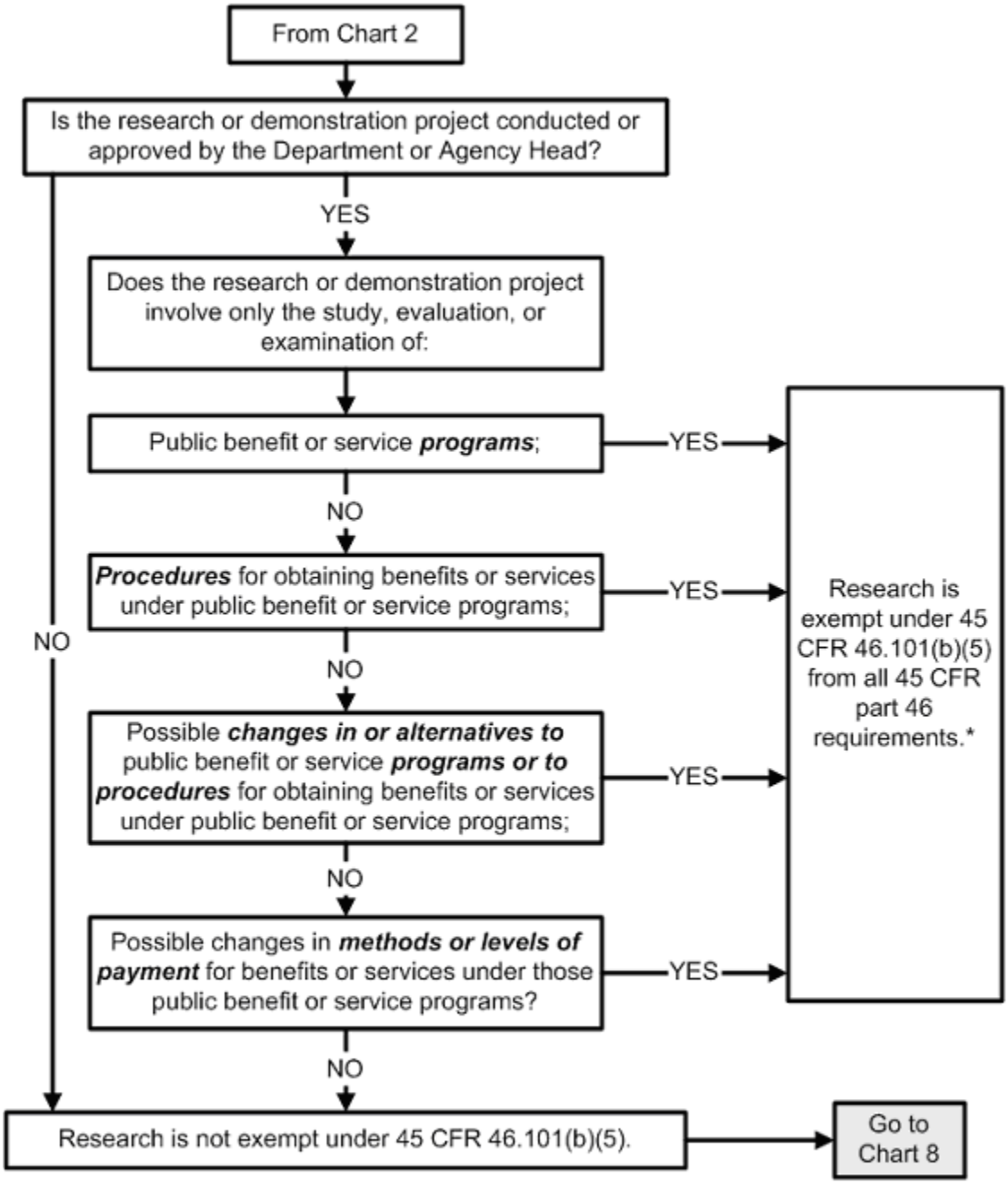
Chart 6: Does Exemption 45 CFR 46.101(b)(5) (for Public Benefit or Service Programs) Apply?



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

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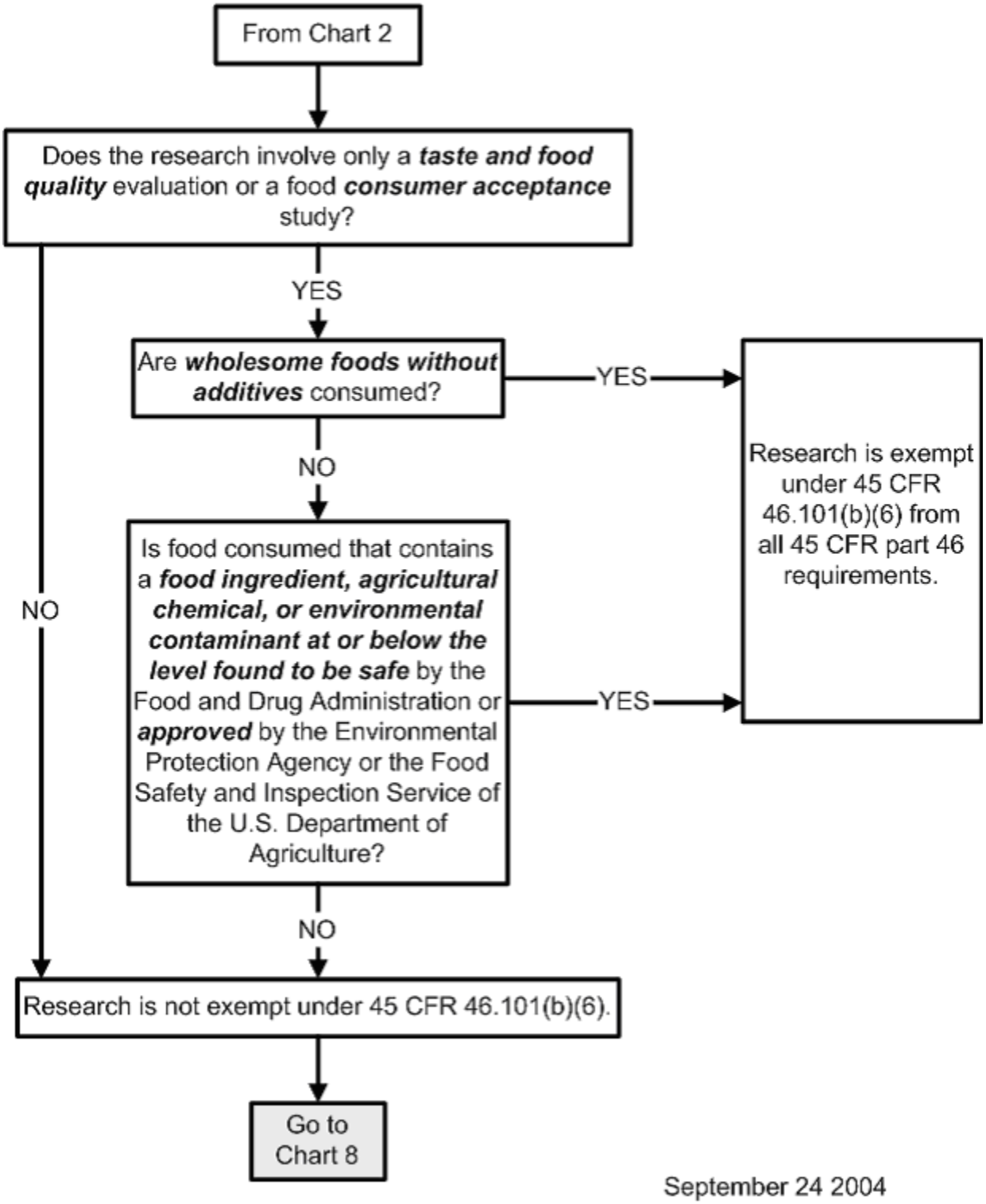
Chart 7: Does Exemption 45 CFR 46.101(b)(6) (for Food Taste and Acceptance Studies) Apply?



September 24 2004

Chart 8: May the IRB Review Be Done by Expedited Procedures Under 45 CFR 46.110?*

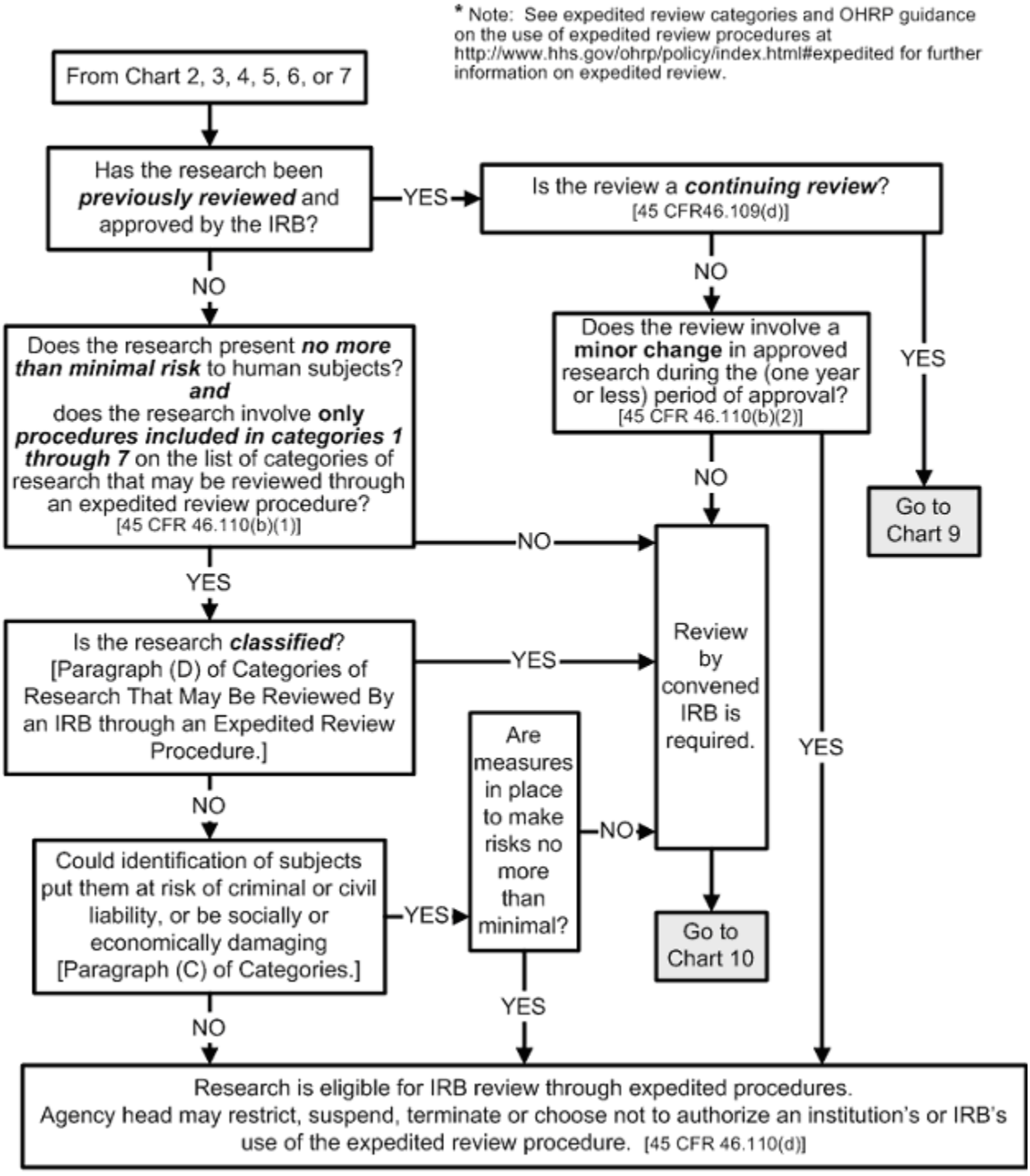


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Chart 9: Can Continuing Review be Done by Expedited Procedures Under 45 CFR 46.110?

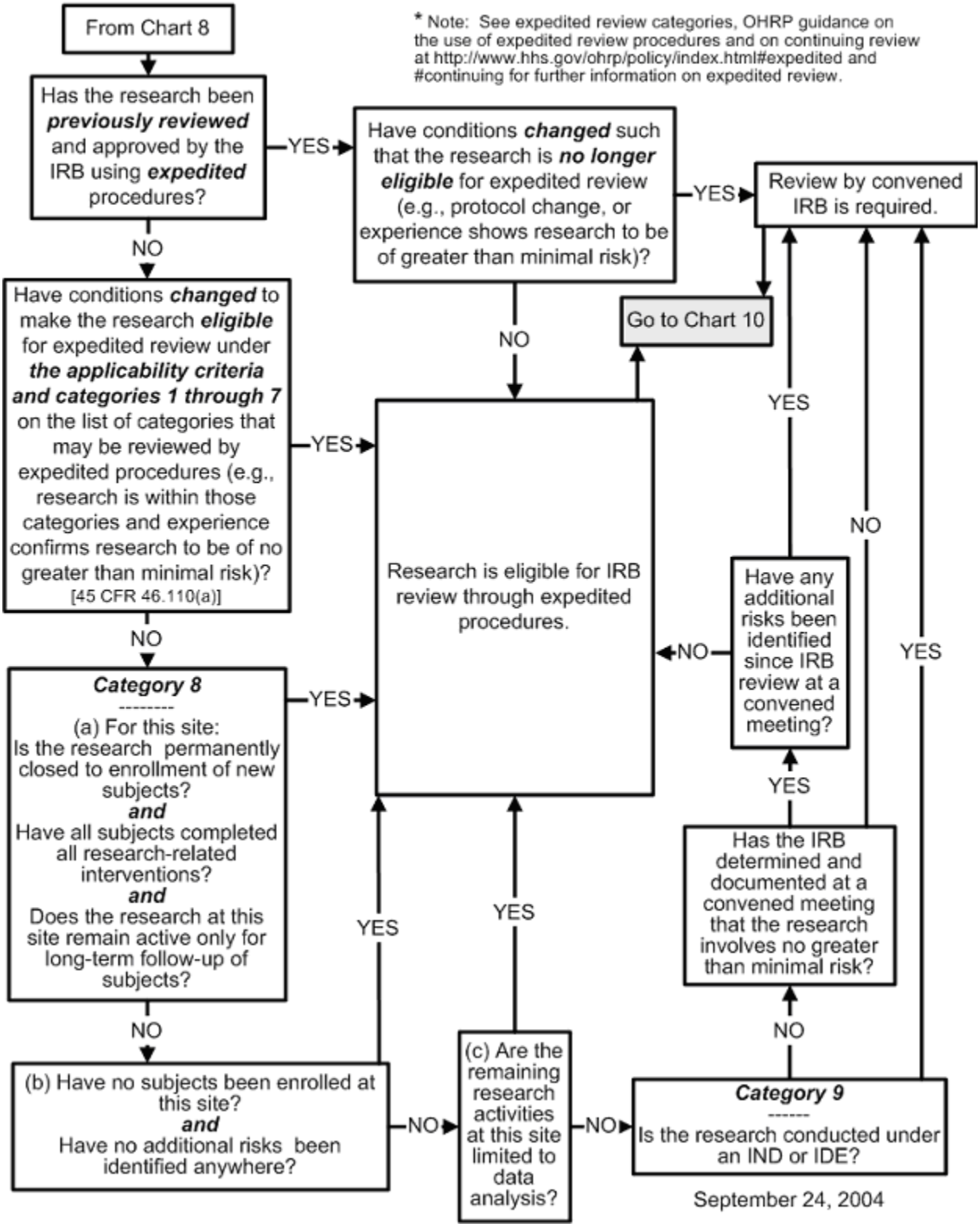
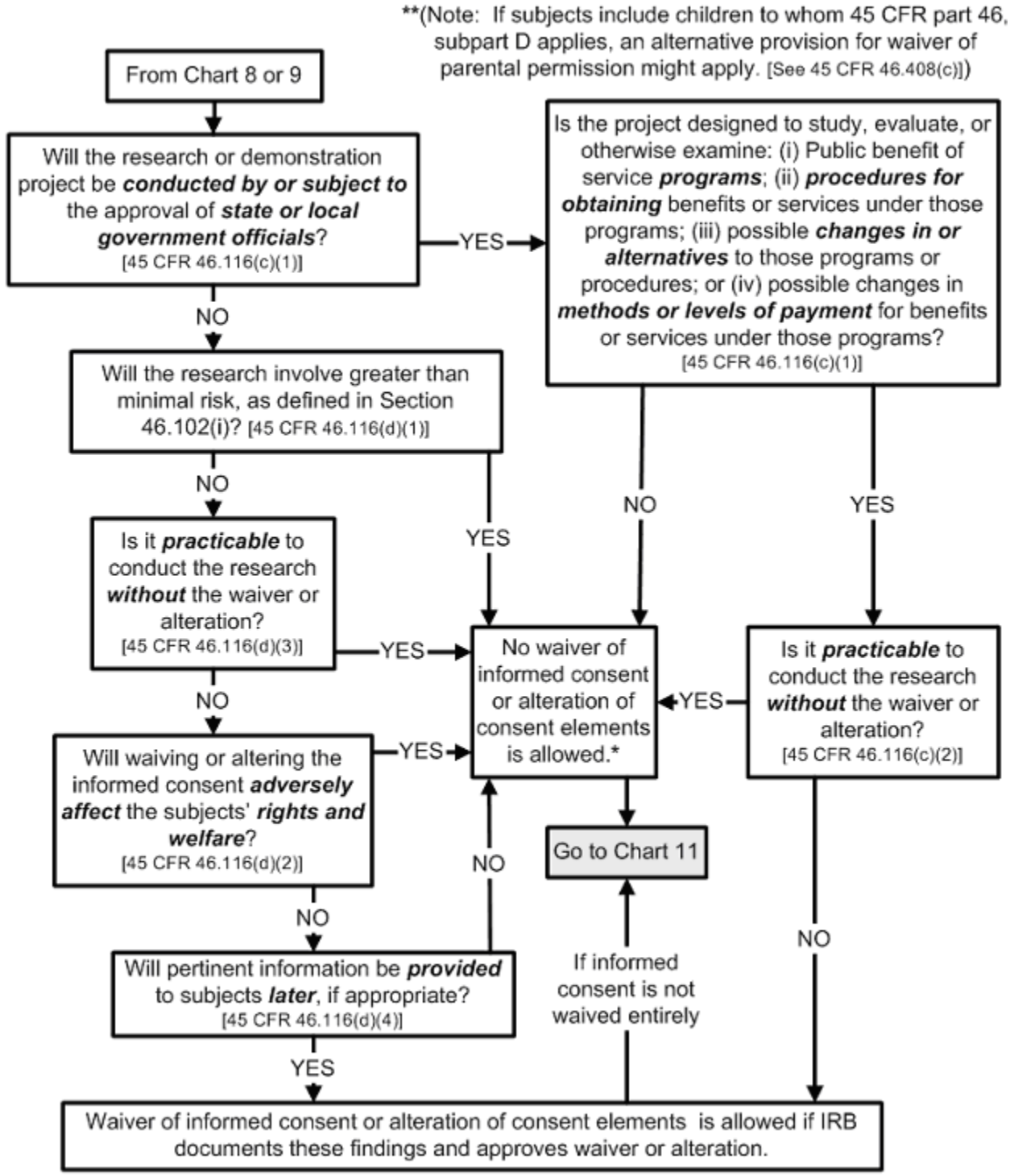


Chart 10: Can Informed Consent Be Waived or Consent Elements Be Altered Under 45 CFR 46.116(c) or (d)?**



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

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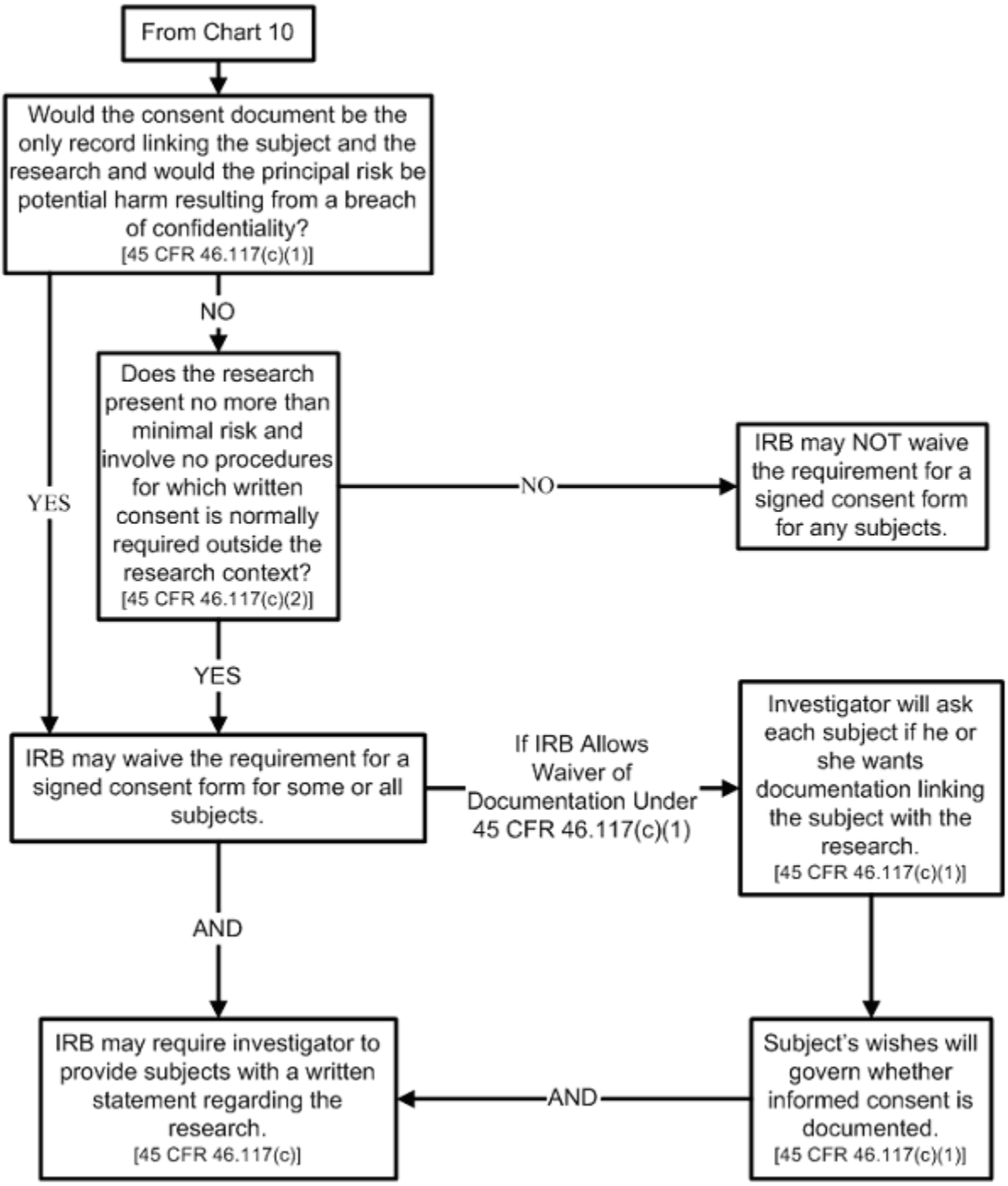
Chart 11: Can Documentation of Informed Consent Be Waived Under 45 CFR 46.117(c)?



September 24, 2004

Appendix C: Informed Consent - Protection of Human Subjects:

Introduction

No clinical investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent from the subject. Informed Consent is a written notification to human subjects involved in clinical investigations that provides them with sufficient opportunity to consider whether or not to participate in the study. The informed consent document must include all the basic elements of informed consent (outlined below) or it may be a short form written consent document stating that the elements of informed consent have been presented orally (§50.27). If the short form method is used, there must be a witness to the oral presentation.

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. The information that is given to the subject or the representative shall be in language understandable to the subject or the representative. 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.

The written consent form must be approved by the Institutional Review Board (IRB) and contain the following basic elements (§50.25):

1. A statement that the study involves research, an explanation of the purposes of the research and the expected 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 who 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.

9. Additional elements of informed consent. When appropriate, one or more of the following elements of information must be provided to each subject:
    a. A statement that a 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.
    b. Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent.
    c. Any additional costs to the subject that may result from participation in the research.
    d. The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject.
    e. A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject.
    f. The approximate number of subject's involved in the study.

The consent form must be signed by the subject or the subject's legally authorized representative. Each signed consent must be maintained by the clinical investigator and a copy of the informed consent must be provided to the human subject.

A combination of oral and written consent may be used. The short form method of informed consent includes a written summary and a "short form." A written summary is a document of what is to be said to the subject or representative and must be approved by the IRB. The summary must include all the basic elements of informed consent (discussed above). A short form is a document stating that the elements of informed consent (§50.25) have been presented orally to the subject or the subject's legally authorized representative.

After oral presentation is provided, the summary must be signed by the witness and the presenter (investigator or investigator's representative). The short form must be signed by the subject (or the representative) and the witness. A copy of the summary must be provided to the subject (or the representative) in addition to a copy of the short form. The signed documents must be maintained by the clinical investigator.

Exception from Informed Consent Requirements for Emergency Research

Criteria for exception from informed consent

There are special cases under emergency care research in which the human subject is in a life-threatening situation and it is not feasible to obtain informed consent. In order to allow such research to proceed, there are special provisions for exception from informed consent requirements (§50.24).

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

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

2. Obtaining informed consent is not feasible because:

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

3. Participation in the research holds out the prospect of direct benefit to the subjects because:

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

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

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

authorized representatives and make this information available to the IRB at the time of continuing review.

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

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

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

<u>IRB Responsibilities</u>

The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document.

The IRB must also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may

discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible.

If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation.

Records of IRB determinations must be retained by the IRB for at least 3 years after completion of the clinical investigation. These records must include the IRB determinations of exemption from informed consent and also the documentation of IRB denial, including documentation of findings and disclosure of the findings to the clinical investigator and the sponsor. The records must be accessible for inspection and copying by FDA [§56.115(b)].

Sponsor Responsibilities

The sponsor must monitor the progress of all investigations involving an exception from informed consent. When the sponsor receives information concerning the public disclosures under (7)(b) and (7)(c) above from the IRB, the sponsor must promptly submit copies of the information that was disclosed to the IDE file and to Docket Number 95S-0158 in the Dockets Management Branch (HFA-305), Food and Drug Administration, 12420 Parklawn Dr., rm. 1-23, Rockville, MD 20857, identified by the IDE number.

The sponsor also must monitor such investigations to determine when an IRB determines that it cannot approve the research because it does not meet the exception criteria or because of other relevant ethical concerns. The sponsor must promptly provide this information in writing to FDA, investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation, and other IRB's that have been asked to review this or a substantially equivalent investigation.

IDE Application

Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IDE is required even if an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments to an approved IDE [§812.35].

References:

21 CFR 50

Information Sheets: Guidance for Institutional Review Boards and Clinical Investigators, 1998
http://www.fda.gov/oc/ohrt/irbs/default.htm

A Guide to Informed Consent
http://www.fda.gov/oc/ohrt/IRBS/informedconsent.html

Frequently Asked Questions on Informed Consent Process and Informed Consent Document Content
http://www.fda.gov/oc/ohrt/IRBS/faqs.html

The Belmont Report, April 18, 1979
http://www.fda.gov/oc/ohrt/irbs/belmont.html

Significant Differences in FDA and HHS Regulations for Protection of Human Subjects
http://www.fda.gov/oc/ohrt/irbs/appendixe.html

Guidance for Institutional Review Boards, Clinical Investigators, and Sponsors: Exception from Informed Consent - Requirements for Emergency Research
http://www.fda.gov/OHRMS/DOCKETS/98fr/000805GL.pdf

Recommended Links

Information for Health Professionals - Clinical Trials and Institutional Review Boards
http://www.fda.gov/oc/oha/default.htm#clinical

Institutional Review Board Guidebook, 1993, National Institutes of Health, Office of Extramural Research, Office for Protection from Research Risks
http://www.hhs.gov/ohrp/archive/irb/irb_guidebook.htm

Document source:
http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/HowtoMarketYourDevice/InvestigationalDeviceExemptionIDE/ucm046766.htm

Appendix D: WCGME-IRB PROTOCOL SUBMISSION FORM (02/09/2004)

Reason for Submission: New Project [ ] Responding to Comment [ ] Reconsideration [ ] Disapproval Resubmission: [ ] Modification [ ] Renewal [ ] Adverse Event Report [ ] **Date of Submission:**	Protocol #:	**IRB Use Only:**

PART A – PROTOCOL/INVESTIGATOR/COORDINATOR INFORMATION
Title of Study:
Principal Investigator: Title of Principal Investigator:
Address of Principal Investigator: Phone number: FAX number: e-mail address:
FAX NUMBER(s) WHERE THE APPROVAL LETTER SHOULD BE SENT: **NOTE: HARD COPIES ARE NOT SENT UNLESS THERE IS NO FAX NUMBER LISTED**
Co-Investigators:
Coordinator's Name: Address: Phone number: FAX number: e-mail address:
PART B – LEVEL OF RISK/TYPE OF REVIEW REQUESTED
Level of Risk: [ ] Minimal [ ] Moderate [ ] High
Type of Review Requested: [ ] Full Board [ ] Expedite
PART C – RECRUITMENT INFORMATION

Number of subjects to be enrolled:
Please note: the IRB considers a subject to be enrolled if s/he signs an informed consent document. If a higher number of subjects must be enrolled for screening in order to hit a targeted number of subjects completing the study, please indicate the higher number.
.

Gender: [ ] Male [ ] Female **Age Range all Subjects:**

Duration of Study Per Subject: **Duration of Study (entire study):**

Site(s) where research procedures will be performed:

PART D – SOURCE OF SUPPORT

Indicate all applicable sources of support and the sponsor:

[ ] Federal – Sponsor:*

*[ ] Commercial** – Sponsor:*

[ ] Foundation – Sponsor:

[ ] Other (specify) – Sponsor

[ ] No support

PART E: CONFLICT OF INTEREST

Does the principal investigator or any co-investigator or research coordinator involved in this study (or in aggregate with his/her spouse, dependents or members of his/her household):

a. possess an equity interest in the entity that sponsors this research or the technology being evaluated that exceeds 5% ownership interest or a current value of $10,000? [ ] Yes [ ] No

b. receive salary, royalty or other payments from the entity that sponsors this research or the technology being evaluated that is expected to exceed $10,000 per year? [ ] Yes [ ] No

c. possess a license agreement with an external entity that would entitle sharing the current or future commercial proceeds of the technology being evaluated? [ ] Yes [ ] No

If yes, please attach detailed information to permit the IRB to determine if such involvement should be disclosed to potential research subjects.

PART F: ADDITIONAL APPROVALS REQUIRED

1. Has this protocol been reviewed by a prior scientific review committee?
   [ ] Yes (Please attach an approval letter) [ ] No (Indicate the reason)

2. Does this research involve the administration, for research purposes, of a drug (investigational or FDA approved)? [ ] Yes* [ ] No
   *(Please attach written notification of receipt/review from the Investigational Drug Service)

3. Does this protocol involve the exposure of human subjects to ionizing radiation (excluding the use of standard diagnostic or treatment procedures, performed in a routine clinical manner and frequency)?
   [ ] Yes (Attach approval letter) [ ] No

PART G: MISCALLANEOUS INFORMATION:

Please provide any additional comments that you feel are necessary for the review of this protocol.

Printed Name and Signature of Principal Investigator: Date

CERTIFICATION OF INVESTIGATOR RESPONSIBILITIES

By signing below I agree/certify that:

1. I have reviewed this protocol submission in its entirety and that I am fully cognizant of, and in agreement with, all submitted statements.

2. I will conduct this research study in strict accordance with all submitted statements except where a change may be necessary to eliminate an apparent immediate hazard to a given research subject.
   - I will notify the IRB promptly of any change in the research procedures necessitated in the interest of the safety of a given research subject.
   - I will request and obtain IRB approval of any proposed modification to the research protocol or informed consent document(s) prior to implementing such modifications.

3. I will ensure that all co-investigators, and other personnel assisting in the conduct of this research study have been provided a copy of the entire current version of the research protocol and are fully informed of the current (a) study procedures (including procedure modifications); (b) informed consent requirements and process; (c) potential risks associated with the study participation and the steps to be taken to prevent or minimize these potential risks; (d) adverse event reporting requirements; (e) data and record-keeping requirements; and (f) the current IRB approval status of the research study.

4. I will not enroll any individual into this research study: (a) until such time that the conduct of the study has been approved in writing by the IRB; (b) during any period wherein IRB renewal approval of this research study has lapsed; (c) during any period wherein IRB approval of the research study or research study enrollment has been suspended, or wherein the sponsor has suspended research study enrollment; or (d) following termination of IRB approval of the research study or following sponsor/principal investigator termination of research study enrollment.

5. I will respond promptly to all requests for information or materials solicited by the IRB or IRB Office.

6. I will submit the research study in a timely manner for IRB renewal approval.

7. I will not enroll any individual into this research study until such time that I obtain his/her written informed consent, or, if applicable, the written informed consent of his/her authorized representative (i.e., unless the IRB has granted a waiver of the requirement to obtain written informed consent).

   - I will employ and oversee an informed consent process that ensures that potential research subjects understand fully the purpose of the research study, the nature of the research procedures they are being asked to undergo, the potential risks of these research procedures, and their rights as a research study volunteer.

8. I will ensure that research subjects are kept fully informed of any new information that may affect their willingness to continue to participate in the research study.

9. I will maintain adequate, current, and accurate records of research data, outcomes, and adverse events to permit an ongoing assessment of the risks/benefit ratio of research study participation.

10. I am cognizant of, and will comply with, current federal regulations and IRB requirements governing human subject research including adverse event reporting requirements.

11. I will make a reasonable effort to ensure that subjects who have suffered an adverse event associated with research participation receive adequate care to correct or alleviate the consequences of the adverse event to the extent possible.

12. I will ensure that the conduct of this research study adheres to Good Clinical Practice guidelines.

Principal Investigator Name (typed)	Principal Investigator signature	Date

Appendix E: Informed Consent Review:

Are the following elements incorporated into the Informed Consent?

A statement that the study involves research.

An explanation of the purposes of the research.

An explanation of the expected duration of the subject's/patient's participation. This should include the length of the study, the number of visits and the length of each visit.

Identification of any procedures that are experimental.

A description of any reasonably foreseeable risks or discomforts to the subject/patient.

A description of any benefits to the subject/patient or to others, which may be reasonably expected from the research.

Payments to volunteers for their participation specifying the amounts and payment schedule under a heading of "Financial Incentives" or "Costs". A proportional schedule should be given in case of subject/patient early withdrawal.

A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be available to the patient. Familiar brand names should be used to describe the procedures or treatments.

A description of the extent, if any, which confidentiality of the subject's/patient's records will be maintained, and disclosure that the sponsor, monitors, auditors, institutional review board (defined as "a committee that has reviewed this research project to help ensure that the rights and welfare of the participants are protected and that the study is carried out in an ethical manner"), the Food and Drug Administration, and any other party authorized by law may inspect the records. If publication of study results is possible, the patient should be advised on the confidentiality of the patient's identity. Advice that confidentiality cannot be guaranteed in either case.

A statement as to whether compensation and/or medical treatments are available, if a research-related injury occurs and, if so, what they consist of, or where further information can be obtained.

Who to contact for information on subject's/patient's rights, (usually the Chairman of the WCGME-IRB), research-related questions, (usually the investigator), and research-related injury (usually the investigator).

A statement that participation is voluntary and refusal to participate will involve no penalty or loss of benefits to which the subject/patient is otherwise entitled.

A statement that the subject/patient may discontinue participation at any time without penalty or loss of benefits to which the subject/patient is otherwise entitled.

When the consent form consists of multiple pages, there should be a designated area on each page prior to the signature page of the consent form where the subject/patient can place their

initials and date of initialing. If the patient is a minor, an area should be provided also for the parent/guardian to initial and date each page.

The protocol title (or short title) should appear on the first page along with the study number.

Pages of the consent form should be consecutively numbered, such as 1 of 4, 2 of 4, etc.

The revision date of the consent form and the study number should appear on each page of the consent form.

When appropriate, one or more of the following elements should also be provided to the subject/patient: Criteria for determining inclusion should involve the research testing of the product, the product's clinical history, and the population under study.

A statement that the particular treatment may involve risks to the subject/patient (or to the embryo or fetus, if the subject/patient is or may become pregnant) which are currently unforeseeable.

Anticipated circumstances under which the subject's/patient's participation may be terminated by the investigator without regard to the subject's/patient's consent.

A description of any additional costs to the subject/patient that may result from participation in the research.

A description of the consequences of the subject's/patient's decision to withdraw from the research and the procedures for orderly termination of participation by the subject/patient.

A statement that significant new findings developed during the research, which may relate to the subject's/patient's willingness to continue participation, will be provided to the subject/patient.

The approximate number of subjects/patients involved in the study.

Appendix F: SAMPLE PATIENT INFORMED CONSENT

Rev. [date] Page I of 4

STUDY TITLE: [Protocol number] - A Double-Blind, Study Comparing ...

STUDY DOCTOR: lnvestigator's Name _____
Address _____
Telephone Number _____

INTRODUCTION:
This consent form is being presented to you, because after a preliminary discussion with this office, you said you were interested in learning more about and possibly participating in this research study. The purpose of this document is to inform you of the purposes of this research, a description of the procedures to be followed, possible risks and discomforts, possible benefits, and of the basic ground rules which will govern this research study. When you have completed reading this form, and if you decide to participate, you may sign the form on the last page, initial and date each prior page and return it to the doctor's office. Please study this form carefully before you make your decision. You may refuse to participate in this study and this decision will not be held against you, nor will it change any matters between you and this office, and you will continue to receive the same medical care.

PURPOSE:
The purpose of this research is to compare the effect of a chemical (_____) solution against a placebo (containing no active ingredient) solution in the treatment of acne, which is a condition of the skin that involves the outbreak of pimples. Acne occurs anywhere on the body, but is usually concentrated on the face, neck, back and chest. The chemical to be studied in this project can kill the bacteria, which are a contributor to the acne condition. If this chemical can help kill the bacteria, it could help improve the acne condition on your body.

PROCEDURE:
If you agree to participate in this ten-week study, you will be required to make five additional visits (every two weeks). Your first visit will determine if you are eligible to be in this study. Most visits will last approximately one hour. Some may be shorter and some may be longer. Sixty volunteers will participate in this study.

To maintain the accuracy of information of this study, the identity of the preparations which will be put on your skin will not be known either to you or the study doctor. This is so an unbiased decision can be made whether or not the chemical is helpful to your condition. Should an emergency occur, the identity of the preparation you are using can be rapidly determined, if needed.

At your first visit, you will be thoroughly questioned about your medical history. Your skin will be examined and the number of pimples will be counted, The doctor will make notes on the medical condition of your skin. You will then be given a bottle of the study preparation which must be applied to the skin on your face twice a day for ten weeks. During the study you may not use any other cleansing products except Purpose soap, and pat your face dry. The study preparation is to be applied in a thin film to the face, paying special attention to the forehead, nose and chin, but avoiding the eyes, nose openings and lips. The preparation is not to be rubbed into the skin and must be kept away from the eyes.

Because it is the property of the company sponsoring the study, all unused study preparation must be returned to the study doctor.

RISKS AND DISCOMFORTS:
Patients who have allergies to sulfur, sulfur compounds, or sulfonamides, may not be included in this study. Pregnant women or nursing mothers are also excluded. You may not participate if you have used other antibiotics on your skin within the past two weeks, or if you have taken antibiotics by mouth within the last four weeks. No other acne medication, including over-the-counter products, or any antibiotics, are permitted to be used by you during the study. The study preparations may cause irritation or dryness of the skin. Some risks may be unforeseeable. Significant new findings developed during the course of the research which may relate to your willingness to continue participation, will be provided to you.

CONTACTS:
If a study related problem should occur, or if you have any questions at any time about the study, contact Dr. _____ at [telephone number]. If you have questions about your rights as a research patient, you may contact Dr. Kenneth H. Rudolph, Chairman of the Institutional Review Board at 570-343-3999. The Institutional Review Board is a committee that has reviewed this research study to help ensure that your rights and welfare as a research patient are protected and that the study is carried out in an ethical manner.

BENEFITS:
By participating in this study, you may or may not experience a decrease in your acne condition. If you are using the inactive preparation or this product fails to work, your condition could become worse.

FINANCIAL INCENTIVES or (COSTS):
Office visits, examinations, procedures, Purpose soap, and study preparations will be at no cost to you. (If applicable, In addition, to help defray the costs of your participation, you 'II be given $50.00 at the last visit for your participation in this study). OR (You will be prequalified with your insurance carrier to determine whether your carrier will cover the costs for this program. The cost of the entire treatment program including both inpatient and outpatient costs will be the responsibility of the patient and/or his or her insurance carrier).

ALTERNATIVE TREATMENT:
You need not participate in this study to receive treatment for your condition. There are over-the-counter products (i.e., Clearasil, Oxy-10, etc.), which have been shown to be effective, in addition to a course of treatment with prescription products (i.e., tetracycline, Retin-A, etc.)

CONFIDENTIALITY:
Your medical records will be kept as confidential as possible under current local, state, and federal laws. However, the personnel associated with this office, representatives of the drug manufacturer, the Food and Drug Administration, possibly other regulatory agencies, the institutional review board, and any other party authorized by law may examine your medical records and the study data. In case the final study data should be prepared for publication, your identity will not be revealed in these manuscripts.

COMPENSATION FOR INJURY:
If a research related injury occurs, the manufacturer of the study drug will pay for immediate treatment, which will be given by the study doctor. However, the drug manufacturer will not pay for treatment of pre-existing conditions or for any treatment of conditions arising after the study.

In addition, you will not receive compensation for wages associated for lost-time at your work place. However, by signing this form you have not given up any of your legal rights.

WITHDRAWAL:
Your participation on in this study is voluntary and, if you decide to withdraw from this study at any time, you may do so without penalty or giving up any benefits to which you are otherwise entitled. You may be terminated from this study by the study doctor for reasons of, but not limited to, (1) a severe adverse reaction, (2) a severe worsening of the condition, or (3) your failure to follow directions.

CONSENT:
I voluntarily agree to participate in this study. I will be given a copy of this signed form.

_____ Participant's Name (printed)	
_____ Participant's Signature	_____ Date
_____ Parent/Guardian Signature	_____ Date
_____ Witness Signature	_____ Date

The Wright Center for Graduate Medical Education
Institutional Review Board
WCGME-IRB

Investigator's Name:_____	Date: _____
Sponsor: _____	Protocol No.: _____
Study Title:	

Our records indicate that your site approval for the above study will expire soon. If you intend to request an extension you must do so using this form. If your study is completed, you must submit your final using this form.

In order to process your request, every question on this form must be complete and signed.
Thank you!

Request for extension: Yes___ No___ **Request to increase number of patients to:** _____

Final Report: Yes___ **No**___ **Is the study permanently closed to enrollment? Yes**___ **No**___

1. Has the study begun?	**Yes**___ **No**___
2. Have all subjects completed all research-related interventions?	**Yes**___ **No**___
Does the research at this site remain active only for long-term follow-up?	**Yes**___ **No**___
3. Number of participants enrolled? _____ Following _____patients?	___ Review in one year. ___ No further review necessary.
4. Have there been any dropouts?	**Yes** ___ (If "yes" you must attach list of subject numbers/initials and reasons for discontinuation.) **No**___
5. Have there been any deaths, hospitalizations, or serious illnesses of study subjects at your site, whether or not they are study related, not reported to the WCGME-IRB?	**Yes**___ (If "yes" you must attach list by subject number/initials, date and event being reported.) **No**___
6. Have there been any changes in the protocol or consent form not reported to the WCGME-IRB?	**Yes**___ (If yes, please attach changes.) **No**___
7. Have there been any changes in the community's attitude toward research since you initially applied to us for approval?	**Yes** ___ (If yes, please attach statements.) **No**___

To be completed by the Principal Investigator or Designee.

Signed: _____ Date: _____

Address: _____

Telephone: _____ Fax: _____

Appendix H: Indemnification Agreement:

INDEMNIFICATION AGREEMENT

Between

_____
Company/Physician Name

And

The Scranton Temple Residency Program - Institutional Review Board (WCGME-IRB)

_____ (Hereafter " _____") agrees to hold harmless, the Scranton Temple Residency Program Institutional Review Board, its principals, agents and board members (WCGME-IRB) from any claims of injury or illness resulting from the evaluation and implementation of Protocol _____, entitled " _____", under the following circumstances:

If any undesirable side effect or reaction occurs following the administration of the product/service or intervention and if WCGME-IRB has employed reasonable care in the evaluation of the protocol, and has not violated any local, state or Federal laws pertaining to medical devices, drugs, biologic agents, or procedures, including, but not limited to, the Federal Food, Drug and Cosmetic Act of 1938, as amended, and the regulations promulgated pursuant thereto, _____ shall indemnify and hold harmless WCGME-IRB against any and all claims, lawsuits, and judgements thereon (including reasonable attorney fees through the appellate level), which may be brought against them as a result of the evaluation or implementation of the protocol.

In the event any such claim is made or lawsuit is initiated, WCGME-IRB shall give prompt written notice to _____, shall permit _____, or its insurance carrier, to defend such claim or lawsuit and shall cooperate fully in any such defense.

WCGME-IRB Accepted by: _____ Signature of Person authorized to legally bind	[Company/Physician Name] By: _____ Signature of Company/Person authorized to legally bind
  _____ Date	 _____ Date

Appendix I: Reporting Requirements for Unanticipated Problems:

Requirements for Reporting Unanticipated Problems that ARE Adverse Events, and Unanticipated Problems that are NOT Adverse Events

Federal Regulation 21CFR §56.108(b)(1) and 45 CFR 46.103(b)(5) require the IRB to "follow written procedures for ensuring prompt reporting to the IRB…any unanticipated problems involving risk to human subjects or others."

An unanticipated problem is defined as any incident, experience, or outcome that meets all of the following criteria:

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

All reports to the IRB of unanticipated problems should explain clearly why the event is "unanticipated" and clearly explain why the event represents a “problem involving risks to human subjects or others.”

Unanticipated Problems that are Adverse Events

Adverse events are any untoward or unfavorable medical occurrence in a human subject, including any abnormal sign (for example, abnormal physical exam or laboratory finding), symptom, or disease, temporally associated with the subject’s participation in the research, whether or not considered related to the subject’s participation in the research.

FDA guidance documents recognize that:

1. “individual adverse event reports generally require an evaluation of their relevance and significance to the study, including an evaluation of other adverse events, before they can be considered to be an unanticipated problem,” and
2. “All reports to the IRB of unanticipated problems should explain clearly why the event described represents a ‘problem’ for the study and why it is ‘unanticipated.’”

FDA believes that reports that lack such evaluation should not be provided to the IRB.

Report to WCGME-IRB only adverse events that in the opinion of the investigator may represent unanticipated problems involving risks to the other subjects in the research.

Investigators are required to report adverse events that fit the following criteria within 10 working days of the time the investigator becomes aware of them:

- Event is 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, or the Investigator Brochure; and (b) the characteristics of the subject population being studied,
- Related or possibly related to participation in the research (possibly related means there is a *reasonable possibility* that the incident, experience, or outcome may have been caused by the procedures involved in the research); and
- Suggests that the research places subjects or others at a greater risk of harm (including physical, psychological, economic, or social harm) than was previously known or recognized.

If the adverse event is clearly not related to the study drug, device, procedures, or washout process, it would not represent a risk to other subjects in the research or a “problem” for the study and, therefore, does not have to be reported to WCGME-IRB.

WCGME-IRB will accept non-site adverse event reports submitted by investigators and from sponsors on behalf of investigators, if, in accord with 21 CFR 312.32,

- the event described is both serious and unexpected,
- the report identifies all previous safety reports concerning similar adverse experiences,
- the report analyzes the significance of the current adverse experience in light of the previous reports, **and**
- the report outlines a corrective action plan (such as a consent form or protocol change).

WCGME-IRB recognizes that for multicenter studies, the sponsor is in a better position to process and analyze adverse event information for the entire study, and to assess whether an occurrence is both "unanticipated" and a "problem" for the study. Accordingly, you may rely on the sponsor's assessment and provide to WCGME-IRB a report of the unanticipated problem prepared by the sponsor.

Reporting Unanticipated Problems that are *Not* Adverse Events

Use the Report Form for Unanticipated Problems that are Not Adverse Events (either "smart form" version or paper version) to report the following unanticipated problems:

- Unanticipated problems that do not fit the definition of an adverse event, but which may, in the opinion of the investigator, involve risk to the subject, affect others in the research study, or significantly impact the integrity of research data. For example, report occurrences of breaches of confidentiality, accidental destruction of study records, or unaccounted-for study drug.
- Unplanned protocol deviations/violations that have already occurred, that may adversely affect the rights, safety or welfare of subjects or the integrity of the research data, AND for which you did not seek WCGME-IRB pre-approval.

Report occurrences within 10 days of becoming aware of them.