PONCE MEDICAL SCHOOL FOUNDATION, INC.
PONCE RESEARCH INSTITUTE

INSTITUTIONAL REVIEW BOARD (IRB)
FOR THE PROTECTION OF HUMAN SUBJECTS

STANDARD OPERATING PROCEDURES

Revised September 2018

TABLE OF CONTENTS

I. Introduction

The Ponce Medical School Foundation (PMSF) Institutional Review Board (IRB) for the Protection of Human Subjects was established to ensure that PMSF complies with all federally mandated regulations which govern research involving human subjects' protection. PMSF's policy is to protect the rights and welfare of all human volunteers who participate in research activities conducted under the auspices of PMSF.

II. Definitions

The IRB has adopted the definitions used by the U.S. Department of Health and Human Services Office for Human Research Protections (OHRP) and the 45 CFR 46:

- *45 CFR 46* - Code of Federal Regulations: Title 45 Public Welfare, Part 46 Protection of Human Subjects is a federal policy that guides the conduct of research involving human subjects.

- *Federalwide Assurance (FWA)* - The FWA is documentation of an institutional commitment to comply with Federal regulations and maintain adequate programs and procedures for the protection of human subjects. It is the principal mechanism for compliance oversight by OHRP.

- *Human subject* - A human subject is a living individual about whom an investigator (whether professional or student) conducting research obtains:
  - Data through intervention or interaction with the individual, or
  - Identifiable private information.

- *Institutional Review Board (IRB)* - A specially constituted review body established or designated by an entity to protect the welfare of human subjects recruited to participate in biomedical or behavioral research.

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

- *Research* - Research is a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge.

III. Institutional Responsibilities

The PMSF IRB follows the rules and regulations of the Commonwealth of Puerto Rico. Additionally, the IRB is certified by the Office for Human Research Protections (OHRP) with an Assurance Number ***FWA 00000345***. The PMSF IRB Registration number is ***IRB 00001027***

A. Federalwide Assurance (FWA)

The FWA is required for all Departments of Health and Human Services (DHHS) funded research involving the use of human subjects. It is a formal commitment made by an institution to provide for the protection of human subjects. Any institution with an FWA agrees to and is responsible for protecting human subjects. PMSF assures that all of its

activities related to human subject's research, regardless of the source of support, will be guided by the ethical principles in the **Belmont Report**.

- *Respect of Persons* - Individuals should be treated as autonomous agents or human beings. Persons with diminished autonomy are entitled to protection.

- *Beneficence* - Persons are treated in an ethical manner not only by respecting their decisions and protecting them from harm, but also by making efforts to secure their well-being. (do not harm; and maximize possible benefits and minimize possible harms).

- *Justice* - The ethical principle requiring that the burden and benefits of research shall be distributed equitable.

PMSF assures that whenever it engages in human subject research conducted or supported by any federal department or agency that has adopted the Federal Policy for the Protection of Human Subjects, known as the **Common Rule,** the Institution will comply with the Terms of the Federalwide Assurance for Institutions within the United Sates (contained in a separate document on the OHRP website), unless the research is otherwise exempt from the requirement of the Common Rule or a department or agency conducting or supporting the research has determined that the research shall be covered by a separate assurance.

B. Institutional Oversight

Within the institution there must be a point of responsibility for the oversight of research and IRB functions. This point should be an official of the institution who has the legal authority to act and speak for the institution and should be someone who can ensure that the institution will effectively fulfill its research oversight function.

The ***Signatory Official,*** according to OHRP, is responsible for "setting the tone for an institutional culture of respect for human subjects". The designated Signatory Official is the President of the Ponce Medical School Foundation.

The ***Human Protections Administrator*** is the primary contact for DHHS OHRP and has administrative responsibility for PMSF Human Protections Administration that includes ensuring that human subjects involved in research are adequately protected and that PMSF remains in compliance with regulations.

IV. Investigator's Responsibilities

A. Principal Investigator

Principal Investigators must have appropriate credentials. They must be faculty members of a clinical department of a hospital or a medical school clinical or basic science department or academic programs. Students in training and professionals in training cannot be Principal Investigators but they can be Co-PI's.

B. Training Courses

The Principal Investigator and all key personnel working on the research project must complete the required human subjects' protections educational trainings prior to beginning the research. Proof of training in the form of a certificate must be supplied to the IRB with the application. IRB applications from investigators who have not completed the required education will be returned without review. PMSF is affiliated with the "Collaborative Institutional Training Initiative (CITI Program) for the provision of online training for our faculty, students and staff (citiprogram.org). Training certificates are valid for three years.

Training courses available are:

- Humans Subject Research
- Good Clinical Practice
- Biosafety-Biosecurity
- Animal Care and Use
- Information Privacy and Security
- Responsible Conduct of Research
- Disaster Planning for the Research Enterprise (DPRE)

C. Submitting Protocols for Approval

All investigators must obtain IRB approval for each research protocol involving human subjects prior to initiating the study by doing the following: *(also refer to Section VI. The IRB Review Process).* **Protocols submitted without all the required documentation will not be reviewed.**

All submissions must be done electronically thru STREAMLYNE System

STREAMLYNE is an efficient online system for faster review and online approval. The primary objective of the implementation of Streamlyne at PMSF is to remove the paper processing related to Research Administration Compliance. We kindly recommend reading the guidelines carefully, answer all of the IRB questions directly related to the protocol needs and save your responses frequently.

Login to Streamlyne

1. Go to https://research.ponce.streamlyne.org
2. PHSU employees can login with your username and password.

If you're not an employee at PHSU and would like to have access to Streamlyne, please send your complete name, email, phone number and institution name to Ms. Rocio Marrero at rmarrero@psm.edu.

D. PMSF IRB rules and regulations

- Consent form, assent form (if applicable), and all supplemental material (flyers, posters, questionnaires, interviews, advertisements) must be submitted both in English and in Spanish. These forms must be written in simple language at an 8th grade reading level.

- Certificates of Human Subjects training and Information Privacy Security: citiprogram.org, (Training certificates are valid for **three** years).
- All protocols involving tissue and DNA sample collection must have the HIPAA Authorization Form.
- Children are defined <21 in Puerto Rico.
- In Puerto Rico, marriage between 18-21 years of age confers full emancipation, giving the power to consent. But under 18 years of age, marriage does not turn a minor into an adult.
- If any vulnerable population (children, prisoners, etc.) is included as subjects in a study, a specific reason for their inclusion should be stated.
- No placebo may be used in children
- All advertisements must be approved in advance by the IRB.
- Overemphasis of benefits to the subjects in the advertisement or consent form is considered coercion.
- Payment is not considered a benefit and should not be put in the Benefits section, but rather in a compensation section.
- Payment should not be pro-rated per visit. Full payment must be given early in the process, even if the subject ends up leaving the study.
- The total amount of the payment must be stated and actually given to all subjects, regardless of their completion of the study.
- Research activities involving institutions and agencies outside of PMSF must receive written approval from the appropriate official within the agency. The written approval must be submitted with the IRB application.
- Justification of exclusion criteria
- Please note the <u>difference</u> between <u>anonymity</u> and <u>confidentiality.</u> An anonymous study does not collect any information that may identify the human subject. If personal information is to be collected, then appropriate measures to protect the privacy and assume confidentiality of the data must be explained.

E. Amendments/Changes to Protocols already approved

The Principal investigator must promptly report proposed modifications to approved studies to the IRB. No changes to the study should be initiated without prior IRB review and approval. Some modifications may require full IRB review.

F. Progress Reports (protocols already approved))

Protocols already approved by IRB must be submitted **at least one time per year** for renewal purposes. At that time the following information must be addressed:

- ❖ Number of subjects
- ❖ Description - any adverse event or problems-How many subjects withdraw
- ❖ Summary of any recent literature since last approval
- ❖ A copy of the currently informed consent form
- ❖ Fill out the "Continuing Review Form"

G. **Safety Mailing Reports Submission:**

The IRB is responsible for reviewing reports of any adverse events or unanticipated problems involving risks to subjects or others. The following must be reported immediately, within 7

calendar days, except where "within 24 hours" if the protocol deviation was made in order to eliminate an apparent immediate hazard to a participant:

Submit a summary page with the SAE's. The summary page would include:

- Patient's coded ID number
- Date of Report
- Kind of report (i.e. Initial, FU#1, etc.)
- Adverse event
- Opinion of Investigator whether or not protocol related. It is very important to write an opinion about the adverse events that are probably or possibly related to the study drugs and what steps, if any, are going to take to minimize risk to patients.

H. Processing Fee

Upon request of protocol review of clinical study supported by Private or Pharmaceutical companies, PMSF-IRB will collect processing fees from either PI or supporting entities.

IRB fee per each protocol submitted:

Full Review	$2,500
Fast-track Review	$3,500
Renewal fee:	$1,200
Expedited review:	$1,500
Exemption review:	$ 500

I. Informed Consents

Investigators must provide a copy of the IRB-approved and stamped informed consent form to each participant at the time of consent. All documentation must be stored as outlined in the IRB application in a secure location for a minimum of three years after the completion of the study.

V. The Institutional Review Board (IRB) for the Protection of Human Rights

A. IRB Authority/Jurisdiction

In accordance with federal guidelines, the IRB has the authority to approve, modify, or disapprove proposed human research studies; authority to modify or disapprove ongoing studies; *no individual in the institution can approve a project that the IRB has disapproved.*

An IRB shall have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects. Any suspension or termination of approval shall include a statement of reasons for the IRB's action and shall be reported promptly to the investigator, appropriate institutional officials, and the department or agency head *(45 CFR 46.113)*

B. Composition

According to federal policy, *45 CFR 46.107*, IRB committee membership shall consist of a minimum of 5 members of diverse backgrounds in regards to race, gender, cultural background, profession, and sensitivities to community issues. The membership should include at least one person who is not affiliated with the PMSF or related to a person who is affiliated with the PMSF. One member shall work in primarily the scientific arena while one should work primarily in the nonscientific arena. The goal is to have a diverse group of members to limit bias in regards to the approval or disapproval of research.

A list of current IRB members must be submitted to OHRP and also kept with the IRB's records *(45 CFR 46.103(b)(3) & 46.115(a)(5).* **The list must identify members by name, earned degrees, representative capacity, indications of experience (such as board certifications and licenses) sufficient to describe each member's chief anticipated contributions to IRB deliberations,** and any employment or other relationship between each member and the institution (i.e., full-time employee, stockholder, unpaid consultant, or board member). Any changes in the IRB membership must be reported to the head of the department or agency supporting or conducting the research, unless the department or agency has accepted the existence of a DHHS-approved Assurance *(45 CFR 46.103(a)).* In the latter case, changes in membership are to be reported to OHRP. (*45 CFR 46.103(b)(3*) and *46.115(a)(5)*

C. IRB Member Considerations

The IRB can have as many members as necessary for it to perform its duties effectively. Care should be taken, however, to ensure that it does not become so large that its management becomes cumbersome.

The nonaffiliated (community) member of the IRB should be drawn from the local community-at-large. Ministers, teachers, attorneys, businesspersons, or homemakers are possible candidates. The person selected should be knowledgeable about the local community. The nonaffiliated members(s) should not be vulnerable to intimidation by the professionals on the IRB, and their services should be fully utilized by the IRB.

An investigator can be a member of the IRB; however, without exception, the investigator-member cannot participate in the review and approval process of any project for which there is a present, potential or perceived conflict of interest. Where there is a conflicting interest, the investigator-member should be present **only** to provide information requested by the IRB. The investigator-member should be absent from the meeting room during the discussion and voting phases of the review and approval process; IRB minutes should reflect whether or not these requirements have been met.

If the IRB regularly reviews research that involves a vulnerable category of subjects, such as children, prisoners, pregnant women, or handicapped or mentally disabled persons, the IRB must consider the inclusion of one or more individuals who are knowledgeable about and experienced in working with these subjects.

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

D. Member Appointment

IRB members are appointed by the President of Ponce Medical School Foundation. Appointments are made on a yearly basis.

E. IRB Member Responsibilities

IRB Members shall:

- Complete the required human subjects' protections educational trainings before beginning their appointment. "Collaborative Institutional Training Initiative" (citiprogram.org).
- Attending workshops and other educational opportunities focused on IRB functions should be encouraged and supported to the extent possible.
- Keep updated with an understanding of the ethical principles of human participant research, federal regulations, applicable state laws, PMSF Federal Wide Assurance (FWA) and institutional policies and procedures for the protection of human participants.
- Review and criticize each proposal submitted and present a summary critique at the IRB meeting
- Abstain from participating in the review, voting or continuing review of a study when he/she has a conflict of interest. the IRB member may be required, however, to provide information to the IRB about such projects
- Keep all information related to the discussions of specific research studies in strict confidence at all times.
- Notify the IRB Chair when he/ she will not attend an upcoming IRB meeting in a timely manner
- Maintain good attendance record. Three consecutive unexcused absences or less than 50% attendance/year will disqualify the person's membership. Members may also be removed by the President of PMSF at any time, given written notice, for due cause (i.e. failure to meet IRB responsibilities, failure to meet educational requirements for human participant research, ethical misconduct, disregard for federal regulations or PMSF policies.)

F. Selection/Responsibilities of the Chairperson

One of the most important actions to be taken in establishing the IRB is selecting the individual who will function as chair. The IRB chairperson should be a highly respected individual from within or outside the institution, fully capable of managing the IRB and the matters brought before it with fairness and impartiality.

The task of making the IRB a respected part of the institutional community will fall primarily on the shoulders of this individual. The IRB must be perceived to be fair and impartial, immune from pressure either by the institution's administration, the investigators whose protocols are brought before it, or other professional and nonprofessional sources.

Duties of the chair:

- Ensures the PMSF and Federal and Commonwealth of Puerto Rico rules are being considered as the committee reviews the planned research proposals
- Be familiar with every protocol that comes before the committee and have a thorough knowledge of policy.
- Be responsible for directing the IRB committee meetings to ensure that the meetings proceed as planned in the agenda

- Decide if a protocol is "exempt" from full board review
- Review & approve (with the input of two other IRB members) research that can be identified within federal guidelines as "expedited", because it involves "no more than minimal risk" to a person who may consent to participate or if there is a small change in a previously approved protocol.
- Review and approve or disapprove any resubmissions of protocols deemed "approval pending clarification/modification" by the full IRB only when the convened IRB has stipulated specific revisions requiring simple consensus by the investigator.
- Identify and assign lead reviewers for protocols to be reviewed by the full board

G. IRB Administrator Responsibilities

The IRB Administrator will work closely with the IRB Chair in matters of developing policy for IRB Committee meetings. The Administrator must have a thorough understanding of federal policy and must work daily to ensure that the PMSF remains in compliance with all applicable federal regulations. A major responsibility is to triage the proposals received into the categories of IRB review (exempt, expedited, or full committee review.)

Record Keeping: The Office of the IRB Administrator must prepare and maintain adequate documentation of IRB activities. In addition to the written IRB procedures and membership lists required by the Assurance process, such documentation must include copies of all research proposals, reviewed, minutes of the IRB meetings, records of continuing review activities, copies of all correspondence between the IRB and investigators and statements of significant new findings provided to subjects.

H. Alternate Members

From time to time, as needed, alternate members may be appointed for a regular voting member(s). The appointment of an alternate member shall be based on expertise similar to that of the regular voting member(s). An alternate member may vote only when the regular voting member is absent.

I. IRB Meetings

The IRB will meet once a month, as needed, to review, discuss and vote on submitted protocols. If there are no protocols to review in any given month, the IRB is not required to meet. From time to time, if there are no protocols to review, the IRB may decide to meet to keep updated on the expedited and exempt protocols that were received. One week prior to each meeting, members will receive submitted protocols for preliminary review. In addition, each IRB member will receive the location, time and date of the meeting.

During a convened meeting, a majority of the members of the IRB must be present including at least one scientist and one nonscientist and one community member. If the required number of members is lost during a meeting, no further action may be taken until it is restored. In order for research to be approved, it must receive the approval of a majority of the voting members present at the meeting.

Minutes of IRB meetings will include attendance; actions taken by the IRB; vote on these actions including the number of members voting for, against, and abstaining; the basis for requiring changes in or disapproving research; and a written summary of the discussion of controverted issues and their resolution.

The IRB will make one of the following four determinations regarding an application:

- **Approved** without questions, concerns or requests for modifications

- **Approval Pending/Conditional** clarification and/or modification of minor specific points or components of the application. The research activity may not be undertaken until the IRB's concerns are addressed and submitted to the designated IRB member or review and approval

- **Deferred (tabled).** This indicates approval by the IRB has been withheld as substantive concerns or significant requests for clarification have been raised and/or the proposed research does not meet PMSF or federal or Puerto Rico guidelines for the protection of human participants. The research activity may not be undertaken until the IRB's concerns are add4essed and submitted to the full IRB for review and approval.

- **Disapproved.** The IRB may disapprove a proposed activity with serious and substantive problems and/or that fails to meet PMSF, Federal or Puerto Rico guidelines for the protection of human participants.

Approval of the proposed research is usually granted for a period of one year commencing on the date of the convened meeting of the IRB at which the protocol was reviewed and approved. Based upon an assessment of the degree of risk to human participants, the IRB may specify special conditions whereby the investigator has a shorter approval period or must report research progress at specific intervals. Continuation of projects past the approval period requires project continuation review and approval by the IRB chair or designee.

VI. The IRB Review Process

A. Review Requirements

The IRB chair or his/her designees will determine whether a given study/protocol can be considered human participants' research based on the federal definition of "research".

The IRB Chair or his/her designees will also determine if certain categories of research involving minimal risk to participants meet one of the Federal categories for expedited review. In these cases, the IRB chair or his/her designee will review the study through expedited review procedures and the entire board need not review the study.

The three basic ethical principles - Respect for Persons, Beneficence, and Justice - set forth in the Common Rule and *The Belmont Report,* shall guide the IRB in its review.

1. Respect for Persons

- Where appropriate, the IRB shall require adequate provisions to protect the privacy of participants and to maintain the confidentiality of data.

- In accordance with *45 CFR 46.111(b*), when some or all of the participants are likely to be vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons, the IRB shall determine whether additional safeguards have been included in the research to protect the right and welfare of these participants.

- The investigator shall seek informed consent from each prospective participant or the participant's legally authorized representative in accordance with and to the extent required by *45 CFR 46.116*, and such consent shall be appropriately documented, in accordance with, and to the extent required by *45 CFR46.117* and retained as a matter of record.

- When research involves more than minimal risk or substantial stress or discomfort, such risk, stress or discomfort shall be carefully explained to the participant before his or her participation and justified b the expected benefits of the research.

- A participant shall have the right to withdraw from a research project at any time or to refuse to participate without loss of benefits to which the individual would otherwise be entitled. In addition, a participant shall have the right to appropriate professional care, to privacy and confidentiality in the use of personal information, and to freedom form undue embarrassment, discomfort, anxiety and harassment.

2. Beneficence

- Direct or potential benefits to the participant or the importance of knowledge to be gained shall not preclude consideration of the inherent risks to the individual.

- The IRB will consider the qualifications of the investigator, his or her professional development, and experience when assessing the degree of risk to participants in the research project. This assessment applies to research that may fall within all categories of IRB review.

- Research plans should make adequate provision for monitoring the data collected to ensure the safety of participants, where necessary.

- Risks to participants shall be minimized by using procedures that are consistent with sound research design.

- Risks to participants shall be reasonable in relation to the anticipated benefits, if any, and the importance of knowledge that may reasonable be expected to result. In evaluating risks and benefits, the IRB shall consider only those risks and benefits that may result from the research (as distinguished from risks and benefits participants would receive even if they were not participating in the research). The IRB shall not consider the long-range effects of applying knowledge gained in the research as among those research risks that fall within the purview of its responsibilities.

3. Justice

- Selection of participants shall be equitable. When appropriate, every effort shall be made to include participants of diverse age, race, gender, and ethnicity.

- The IRB shall ensure that compensation or inducement offered for participation in a study is made appropriately, with participants fairly recruited and adequately informed rather than unduly influenced by promised compensation. Financial incentives should not be so great as to be coercive to potential participants and should constitute reasonable compensation for the inconvenience of participating. Information related to compensation shall be included in the informed consent form.

- No recruitment or involvement of human participants in research shall be permitted until the IRB has reviewed and approved the research application and informed consent has been obtained. It is the principal investigator's responsibility to obtain approval from the IRB prior to the initiation of any research, including pilot or pre-test studies, involving the use of human participants.

- The investigator should ensure that consent for participation is sought only under circumstances that minimize the possibility of coercion or undue influence. Subject participation must be voluntary, and the subject should be able to withdraw from the study at any time without penalty.

B. Criteria for IRB Approval of Research

(45 CFR 46.111) (a) in order to approve research covered by this policy the IRB shall determine that all the following requirements are satisfied:

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

- Risks to subjects are reasonable in relation to anticipated benefits, if any, to subjects, and the importance of the knowledge that may reasonably be expected to result. In evaluating risks and benefits, the IRB should consider only those risks and benefits that may result from the research (as distinguished from risks and benefits of therapies subjects would receive even if not participating in the research). The IRB should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among those research risks that fall within the purview of its responsibility.

- Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should b particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

- Informed consent will be sought from each prospective subject or the subject's legally authorized representative, in accordance with, and to the extent required by

45 CFR 46.116.

- Informed consent will be appropriately documented, in accordance with, and to the extent required by *45 CFR 46.117.*

- When appropriate, the research plan makes adequate provision for monitoring the data collected to ensure the safety of subjects.

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

C. Levels of Review

1. Exempt Review

The following research activities are considered exempt from federal regulations as stated in *45 CFR 46.101(b):*
Unless otherwise required by department or agency heads, research activities in which the only involvement of human subjects will be in one or more of the following categories are exempt from this policy:

- Research conducted in established or commonly accepted educational settings, involving normal educational practices, such as (i) research on regular and special education instructional strategies, or (ii) research on the effectiveness of or the comparison among instructional techniques, curricula, or classroom management methods.

- Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures or observation of public behavior, **unless:**

    - Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and

    - Any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

- Research involving the use of educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior that is not exempt under paragraph (b)(2) of this section, **if:**

    - The human subjects are elected or appointed public officials or candidates for public office; or

    - Federal statute(s) require(s) without exception that the confidentiality of the personally identifiable information will be maintained throughout the research and thereafter.

- Research involving the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens, if these sources are publicly available or if the information is recorded by the investigator in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.

- Research and demonstration projects which are conducted by or subject to the approval of department or agency heads, and which are designed to study, evaluate, or otherwise examine:

    - Public benefit or service programs; (ii) procedures for obtaining benefits or services under those programs; (iii) possible changes in or alternatives to those programs or procedures; or (iv) possible changes in methods or levels of payment for benefits or services under those programs.

- Taste and food quality evaluation and consumer acceptance studies, (i) if wholesome foods without additives are consumed or (ii) if a food is consumed that contains a food ingredient at or below the level and for a use found to be safe, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the Food and Drug Administration or approved by the Environmental Protection Agency or the Food Safety and Inspection Service of the U.S. Department of Agriculture. *45 CFR 46.101(b)*

2. Expedited Review

Expedited review categories of research shall comply with "Categories of Research That May be Reviewed by the IRB through an Expedited Review Procedure". *63 FR 60364-60367, November 9, 1998*

- Clinical studies of drugs and medical devices only when condition (a) or (b) is met. (a) Research on drugs for which an investigational new drug application (21 CFR Part 312) is not required. (b) Research on medical devices for which (i) an investigational device exemption application (21 CFR Part 812) is not required; or (ii) the medical device is cleared/approved for marketing and the medical device is being used in accordance with its cleared/approved labeling.

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

- Prospective collection of biological specimens for research purposes by noninvasive means.

- Collection of data through noninvasive procedures (not involving general anesthesia or sedation) routinely employed in clinical practice, excluding procedures involving x-rays or microwaves. Where medical devices are employed, they must be cleared/approved for marketing. (Studies intended to evaluate the safety and effectiveness of the medical device are not generally eligible for expedited review, including studies of cleared medical devices for new indications.)

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

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

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

- Continuing review of research previously approved by the convened IRB as follows: (a) where (i) the research is permanently closed to the enrollment of new subjects; (ii) all subjects have completed all research-related interventions; and (iii) the research remains active only for long-term follow-up of subjects; or (b) where no subjects have been enrolled and no additional risks have been identified; or (c) where the remaining research activities are limited to data analysis.

- Continuing review of research, not conducted under an investigational new drug application or investigational device exemption where categories two (2) through eight (8) do not apply but the IRB has determined and documented at a convened meeting that the research involves no greater than minimal risk and no additional risks have been identified.

The IRB may use the expedited review procedures to review minor changes in previously approved research during the period for which approval is authorized.

The expedited review procedure is carried out by the IRB chair and his/her designees.

In reviewing the research, reviewers may exercise all of the authorities of the IRB except the reviewers may not disapprove the research. Disapproval of a research application requires the majority of the fully IRB.

At a convened IRB meeting, members may request that certain protocols be approved by the IRB in accordance with full board review procedures. A vote of the members shall be taken concerning the request and the majority shall decide the issue. A PI may also request that an application receive full board review.

The IRB Chair shall review amendments for previously approved research which can be approved under an expedited review procedure.

3. Full Board Review

All proposed research deemed by the IRB chair to fit neither the exempt or expedited review must be reviewed by the full IRB. In addition, the IRB may require full review of any research submitted or approved under expedited review and any research not approved by expedited review.

The primary criteria for full board review are the risk to participants during the procedures and interactions between participants and researchers.

Examples of research activities that must be reviewed by the full IRB include:

- Research in which potential participants may not be given sufficient information to make decisions about whether to participate and accept potential risks. This may include research in which outright deception or incomplete disclosure of the purpose of the study might reasonably affect a person's decision to participate in the study

- Research involving more than minimal risk, where defined as "the probability and magnitude of harm or discomfort are not greater in and of themselves than those ordinarily encountered in the daily life or during the performance of routine physical psychological examinations or tests"

- Non-curricular, interactive research in primary and secondary schools.

- Research in which participation per se in the study constitutes a risk (i.e. identification as a participant in a drug-use survey). This would include research in which researchers have applied for a waiver of documentation of consent, which can be used as a method of reducing risks to participants who may be placed at risk simply by being involved in the study.

- Research on special populations, i.e., minors, prisoners, pregnant women and mentally incompetent persons.

- Research involving potential risks to participant's right to privacy and /or threats to confidentiality.

4. Continuing Review

The IRB is required to re-evaluate research projects at appropriate intervals not less than **once a year**. For research involving no more than minimal risk, the approval period is generally one year from the date of the convened meeting at which the protocol was reviewed ad approved. For research involving greater than minimal risk, the IRB will determine the appropriate approval period.

Investigators are required to submit progress reports to the IRB before the expiration date of the study.

An original protocol may have received an expedited review, but the continuing review may go to the full IRB, as deemed necessary by the IRB Chair or a designee.

Continuing review is required for continued analysis of identifiable information but is <u>not required</u> if the data have been de-identified.

- For new analysis of previously collected identifiable data, a new IRB protocol is required.

- For a new analysis of previously collected de-identified data, no IRB review is required.

5. **Case Studies**

A ***Case Study*** is understood to mean the collection and presentation of detailed information about a particular participant or small group, frequently including the accounts of subjects themselves. A form of qualitative descriptive research, the case study looks intensely at an individual or small participant pool, drawing conclusions only about that participant or group and only in that specific context. It may involve collecting data about participants using participant and direct observations, interviews, protocols, tests, examinations of records, and collections of writing samples. Case studies may also involve either retrospective or prospective study. A *retrospective case study* looks backwards and examines the incidence of certain factors in relation to an established outcome. A *prospective case study* looks forward and examines a particular individual or case for a particular outcome that may be associated with the presence/absence of relevant factors.

IRB Review of Case Studies: Case studies generally fail to meet the federal definition of research because there is no intent to test a hypothesis via systematic analysis. As a result, case studies generally qualify for exempt review by the IRB provided that the study (a) does not involve a sensitive topic, (b) is conducted in a manner that protects subjects' identity, and (c) does not involve at-risk or special populations. A listing of privacy issues and special populations are provided below.

Subject private and/or medical identifiers: Exempt studies may not include any of the following identifiers (see Privacy Rule [45 CFR46.514(B)(2)]).

- Names
- All elements of dates (except year) for dates related to an individual, including birth date, admission date, discharge date, or date of death
- All geographic subdivisions smaller than a State, including street address, city, county, precinct, zip code, and their equivalent geocodes
- Telephone numbers
- Fax Numbers
- Electronic mail addresses
- Social security number
- Medical Record numbers
- Health Plan beneficiary numbers
- Account numbers
- Certificate/license numbers
- Vehicle identifiers and serial numbers, including license plate number
- Device identifiers and serial numbers
- Web Universal Resource Locators (URLs)
- Internet Protocol (IP) address numbers
- Biometric identifiers, including finger and voice prints
- Full face photographic images and any comparable images
- Any other unique identifying number, characteristic or code

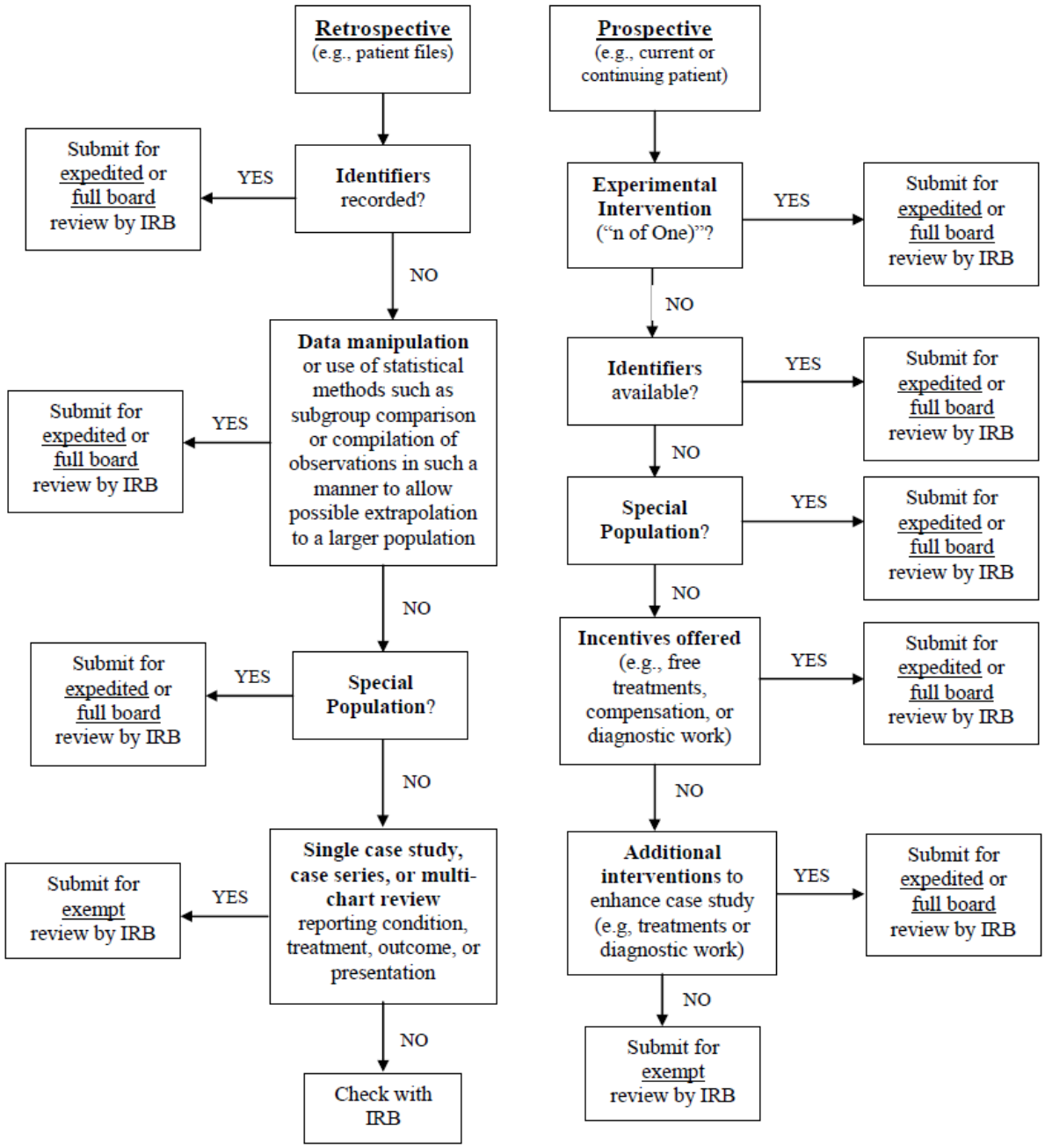
Special populations: Exempt studies may not include participants from any of the following protected groups:

- Pregnant women, human fetuses, and neonates [45 CFR 46 Subpart B]
- Prisoners [45 CFR 46 Subpart C]
- Children [45 CFR 46 Subpart D]

IRB Review of "N of one" Studies and Case Series with Data Manipulation: It is noted, however, that an "N of one" trial that uses an experimental treatment on a single subject, or a case series that incorporates levels of data manipulation (statistics) to allow possible extrapolation of the results to a larger population, would satisfy the federal definition of research. As such, these studies must be submitted to the IRB for expedited for full board review.

Case Study/Case Series

Research or Non-Research Decision Tree for IRB Submission



D. Informed Consent Process

Informed consent must be sought from each prospective participant or participant's legally authorized representative before research is begun. Consent is a continuing process and participants always retain the right to withdraw from participation in a research project. Federal policy requires that investigators inform participants of any important new information that might affect their willingness to continue participating in the research.

1. The basic elements of informed consent as stated in *45 CFR 46.116* are:

   - A statement that the study involves research.
   - An explanation of the purpose of the research.
   - The expected duration of the subjects' participation.
   - A description of the procedures to be followed and, if appropriate, identification of any procedures that are experimental (i.e., therapies that are being tested).
   - A description of any benefits to the participants or to others which may reasonably be expected from the research and how that will contribute to the field of study or may benefit others.
   - A disclosure of appropriate alternative procedures or courses of treatment, if any, that may be advantageous to the participant, description of foreseeable risks or discomfort to the subject.
   - A statement describing the extent, if any, to which confidentiality of records identifying the participant is maintained. This includes the matter and place of data storage.
   - For research involving more than minimal risk, an explanation as to whether any compensation is available, and an explanation as to whether any medical treatments are available if injury occurs and what they consist of or where further information may be obtained.
   - An explanation of whom to contact for answers to pertinent questions about the research and research participant's rights, and whom to contact in the event of a research-related injury. PMSF consent forms should include the address, phone number and e-mail addresses for the PI and the PMSF IRB.
   - A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the participant is otherwise entitled, and the participant may discontinue participation at any time without penalty or loss of benefits to which the participant is otherwise entitled.

2. Additional requirements may include:

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

   - Anticipated circumstances under which participation may be terminated by the investigator without regard to the participant's consent.

   - Any additional costs to the participant that may result from participation in the research.

   - The consequences of a participant's decision to withdraw from the research and procedures for orderly closure of participation by the participant.

   - A statement that significant new findings developed during the course of the research, which may relate to participants' willingness to continue participation, will be provided to the participant.

   - The approximate number of participants involved in the study

   The IRB may waive written documentation of informed consent if (*45 CFR 46.116 c. & d.).*

   - The research represents no more than minimal risk of harm to participants
   - The waiver or alteration will not adversely affect the rights and welfare of the participant
   - The research cold not be carried out without the waiver or alteration, and,
   - Where informed consent constitutes the only threat to anonymity, and
   - Whenever appropriate, the participant will be debriefed.

   Waiver of documentations will be on a case by case basis.

   When consent is waived, the IRB may require the investigator to offer participants written information about the study.

   Consent forms should avoid jargon and should be written in the second person (e.g., If you agree to the research….) in a language and at a level that is understandable to the participant. Informed consent will not be accomplished unless the requirement is met that the participant understands the components of the consent form.

   The person who signs the consent form must be given a copy as a reference and reminder of the information conveyed by the researcher. Non-written methods of administering consent are also possible.

3. Informed Consent for Minors

   Children (minors) are defined as persons who have not attained the legal age for consent to procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. In Puerto Rico, residents under 21 years of age are considered minors unless they are "emancipated" by court order.

Assent is the child's affirmative agreement to participate in research. A child's legal guardian or parent must sign an informed consent form in order for a child to participate in a research study. Where appropriate, the child should assent to participate in the research. Both consent and assent forms must be submitted to the IRB for approval. If assent will not be used, an explanation for not including this component should be included in the application.

4. Informed Consent for Non-English Speaking Subjects

   DHHS regulations for the protection of human participants require that informed consent information be presented "in language understandable to the subject" and, in most situations, that informed consent be documented in writing.

   The written consent document should embody, in language understandable to the participant, all the elements necessary for legally effective informed consent. Participants who do not speak English should be presented with a consent document written in a language they understand. The IRG must receive a copy of the document.

   In the case of the PMSF IRB, Informed Consent Documents must be written in both Spanish and English. If the ICD's come from the states, the translated Spanish ICD must be accompanied with a translation certificate.

E. Modifications

All modifications/amendments to currently approved research must be reviewed and approved by the IRB before implementation. The PI must submit all changes to the IRB. Changes that do not increase the risk to research participants may receive an expedited review. Modifications to approved research projects that are more than minimal risk and do not qualify for expedited review must be forwarded to the full IRB for review and, if appropriate, to those participating in the study by way of a revised informed consent.

The PI shall incorporate each approved modification to a research protocol or consent document into the approved protocol to ensure that there is only one complete protocol, with the revision dates noted. The PI will send a copy to the IRB.

F. Adverse Events and Serious Adverse Events (SAE)

Adverse events and *serious adverse events* involving risks to participants or others are events or problems that are undesirable, unintended, and is harmful or detrimental to the welfare of study participants or other individuals involved with a research study. Reportable events are not limited to physical injury, but include psychological, social, and emotional harm or injury.

All adverse events and unanticipated problems involving risks to participants and others must be reported by the investigator immediately to the IRB. In addition, the investigator is responsible for reporting the event as required by Federal regulation, grant requirements, or contract.

The IRB is responsible for reviewing reports of any adverse events or unanticipated problems involving risks to subjects or others. Upon the receipt of the report, the IRB will determine

whether the study should be modified to reduce the level of risk to participants, or whether the consent form should be modified to include a description of the event.

G. Closure of Approved Research

If an investigator terminates the study, the investigator shall notify the IRB.

Once the PI has terminated the research and so notified the IRB, he or she may not recruit or enroll human research participants. There can be no intervention, interaction or follow-up with enrolled human participants, nor any continued collection of data or analysis of data previously collected as part of the research protocol.

H. Noncompliance

The IRB shall be responsible for reviewing and determining all issues of serious or continuing noncompliance with 45 CFR 46, IRB requirements, or PMSF requirements. Any serious or continuing noncompliance will be reported to the Human Protections Administrator and the IRB Chair who together will investigate all credible reports of alleged noncompliance and inappropriate involvement of human participants in research.

Noncompliance includes: Conducting research without IRB review, not obtaining consent; using the wrong consent form, failing to report adverse events or serious adverse events or other problems, failure to maintain adequate records, failure to follow the IR approved protocol, modifying an approved protocol without IRB approval, inadequate supervision, or inadequate training.

When a report of alleged noncompliance is received by the IRB or Office of Human Subject Protection (OHSP), a preliminary investigation will be undertaken and a determination will be made as to whether participants are at risk or can be allowed to continue in the research while the investigation continues. If subjects are deemed to be at risk the IRB or Human Protections Administrator may ask the PI to temporarily stop the study.

The IRB shall send a letter to the PI citing the alleged areas of noncompliance and the associated federal regulations and asking the PI to respond to the allegation and provide a corrective action plan within a specified timeframe and /or asks the PI to attend a meeting with the IRB Chair, the Human Protections Administrator and any other PMSF administrator that is deemed necessary.

Actions the IRB may take:

- The IRB may determine that the research study is in compliance with federal regulations and IRB policy and no further action is necessary.

- The IRB may decide that the PI found in noncompliance should not be allowed to process new protocols or renew current projects until all concerns have been addressed.

- The IRB may determine the research study under review is substantially in compliance with federal regulations and IRB policy but may make specific recommendations to

improve or enhance the protections for the study's human participants or increase oversight of the project.

I. Suspension or Termination of Research

The IRB has the authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's' requirements or that has been associated with unexpected harm to participants. *(45 CFR 46.113)*

The PI will receive a written notice with the reasons for terminating/suspending his/her study.
The IRB has the authority to re-open terminated projects if it deems this action is necessary and in the best interests of the participants.

J. Appealing an IRB Decision

If the IRB makes a decision that an investigator believes to be unfair or unsubstantiated about his or her proposed research, the investigator should first discuss the matter with the IRB Chair. The investigator should be prepared to present reason that he or she believes that the proposed research is in compliance with PMSF policy, Federal regulations and Puerto Rican Law for the protection of human participants.

If the issue cannot be resolved satisfactorily by negotiation, the PI may appeal the decision, in writing, to the full IRB. The results of any negotiations that require approval by the full IRB will be taken to the next convened meeting for decision and vote.

The investigator may appear before the IRB to present his or her appeal and any supportive material or documentation obtained through consultation, but the investigator cannot be present during the vote on the IRB's final recommendation.

VII. Special Categories

A. Cooperative Research

PMSF will ensure that any of its collaborating entities also possesses mechanisms to protect human participants that are at least equivalent to those procedures provided for in the ethical principles to which PMSF is committed.

PMSF may enter into a joint review arrangement called an *IRB Authorization Agreement*, where it relies upon the review of another qualified IRB with similar standards of human participants' protection, or make similar arrangements to meet IRB review requirements and eliminate duplication of effort. Such arrangements must be (a) in writing, (b) approved and signed by the Signatory Official of the school, which is the President/Dean of PMSF, and (c) approved and signed by correlative officials of the cooperating institutions. These arrangements may be entered into on a case-by case basis.

B. International Research

OHRP works to ensure that human subjects outside of the United States who participate in research projects conducted or funded by DHHS receive the same level of protections as research participants inside the United States. To that end, the OHRP International Activities program offers consultation services, disseminates pertinent reports, and provides research ethics training.

The International Compilation of Human Subject Protections is a listing of 1,000 laws, regulations, and guidelines on human subjects protections in over 100 countries and from several international organizations. Many of the listings embed hyperlinks to the source document. These laws, regulations, and guidelines are classified into six categories:

- General
- Drugs and Devices
- Privacy/Data Protection
- Human Biological Materials
- Genetic Issues
- Embryos, Stem Cells, and Cloning

C. Internet Research

Internet research can include: recruiting participants over the internet and gathering data over the internet.

- *Recruiting over the WEB*. Unsolicited email messages to multiple users are prohibited by PMSF without prior approval. The IRB must review the text of the recruitment script to be presented to participants and the context in which the recruitment takes place

- *Gathering Data.* This type of research involves having participants submit data (i.e., survey data) over the internet and presents the most serious human participants concerns (i.e., obtaining consent, particularly assent from minors) due to the potential limits to confidentiality. The investigator must inform the IRB of how he/she intends to obtain consent.

D. Incomplete Disclosure and Deception in Research

Deception is a method used in social science research that can improve the internal validity of a research study. The intention of deception is to produce a false belief in the participants during the course of the study. Incomplete disclosure of information may also be used in research where telling the subject about some aspect of the study in detail might interfere with the ability to measure the outcome of interest. The use of deception and incomplete disclosure in human subjects research raises special problems for the IRB to consider with regard to informed consent and analysis of risks and benefits. Unethical uses of deception in research can cause distress to those being deceived, and may undermine public trust in the research enterprise.

When studies use deception or incomplete disclosure in their procedures, the IRB needs to determine whether the deception/incomplete disclosure is necessary to make the research scientifically valid and feasible. The IRB will consider whether the study population is appropriate for the study procedures that involve deception or incomplete disclosure of

information, and will consider potential harms of these methods. The IRB never allows for deception/incomplete disclosure that might affect the subject's willingness to participate in the study.

E. Privacy Protection

The National Institutes of Health has made the following determinations in regards to protections privacy; "*Certificates of Confidentiality* are issued by the National Institutes of Health (NIH) to protect identifiable research information from forced disclosure. They allow the investigator and others who have access to research records to refuse to disclose identifying information on research participants in any civil, criminal, administrative, legislative, or other proceeding, whether at the federal, state, or local level. Certificates of Confidentiality may be granted for studies collecting information that, if disclosed, could have adverse consequences for subjects or damage their financial standing, employability, insurability, or reputation. By protecting researchers and institutions from being compelled to disclose information that would identify research subjects, Certificates of Confidentiality help achieve the research objectives and promote participation in studies y assuring confidentiality and privacy to participants." The Office for Human Subject Protection can help with this application process.

Examples of research that can be considered sensitive include:

- Information relating to sexual attitudes, preferences, or practices
- Information relating to the use of alcohol, drugs, or other addictive products
- Information pertaining to illegal conduct
- Information that if released could reasonable be damaging to an individual's financial standing, employability, or reputation
- Information that would normally be recorded in a patient's medical record, and the disclosure of which could reasonable lead to social stigmatization or discrimination
- Information obtaining to an individual's psychological well-being or mental health
- Genetic information

E. Research involving the Gene Pool (DNA)

Issues to Consider in the Research Use of Stored Data or Tissues:

- **Human Tissue Repositories** collect, store, and distribute human tissue materials for research purposes. Repository activities involve three components: (i) the **collectors** of tissue samples; (ii) the **repository** storage and data management center; and (iii) the **recipient** investigators.
- If supported by the Department of Health and Human Services (HHS), each component must satisfy certain **regulatory requirements**.

- Operation of the Repository and its data management center should be subject to **oversight by an Institutional Review Board (IRB)**. The IRB should review and approve a protocol specifying the conditions under which data and specimens may be accepted and shared, and ensuring adequate provisions to protect the privacy of subjects and maintain the confidentiality of data. The IRB should also review and approve a sample collection protocol and informed consent document for distribution to tissue collectors and their local IRBs. A **Certificate of Confidentiality** should be obtained to protect confidentiality of repository specimens and data.

VIII. CERTIFICATE OF CONFIDENTIALITY

Eligibility for a Certificate

1. **Who may apply for a Certificate of Confidentiality?** Any Investigator conducting research in which sensitive information is gathered from human research participants (or any Investigator who intends to engage in such research) may apply for a Certificate of Confidentiality. Note there are other eligibility requirements (see FAQ Section C. Eligibility for a Certificate)

2. **What kind of research is eligible for a Certificate?** Generally, any research project that collects personally identifiable, sensitive information and that has been approved by an IRB operating under either an approved Federal-Wide Assurance issued by the Office of Human Research Protections or the approval of the Food and Drug Administration is eligible for a Certificate. Federal funding is not a prerequisite for an NIH-issued Certificate, but the subject matter of the study must fall within a mission area of the National Institutes of Health or the Department of Health and Human Services.

3. **Can you give some examples of research projects that are eligible for a Certificate?**

   The following is an illustrative but not exhaustive list of research areas eligible for a Certificate:

   - Research on HIV, AIDS, and other STDs;
   - Studies that collect information on sexual attitudes, preferences, or practices;
   - Studies on the use of alcohol, drugs, or other addictive products;
   - Studies that collect information on illegal conduct;
   - Studies that gather information that if released could be damaging to a participant's financial standing, employability, or reputation within the community;
   - Research involving information that might lead to social stigmatization or discrimination if it were disclosed;
   - Research on participants' psychological well-being or mental health;
   - Genetic studies, including those that collect and store biological samples for future use;
   - Research on behavioral interventions and epidemiologic studies.

4. **What studies would NOT be eligible?**

   Ineligible studies include projects that are

- not research based,
- not approved by an IRB operating under either an approved Federal- Wide Assurance issued by the Office of Human Research Protections or the approval of the Food and Drug Administration,
- not collecting sensitive information or information that, if released publicly, might harm the research participants,
- not collecting personally identifiable information, or
- not involving a subject matter that is within a mission area of the National Institutes of Health or the Department of Health and Human Services.

Certificate of Confidentiality vs Other Privacy and Data Protections

Does the Privacy Rule preclude the need for Certificates of Confidentiality?

No. Certificates of Confidentiality offer an important protection for the privacy of research study participants by protecting identifiable health information from forced disclosure (e.g., by court order). While the Privacy Rule does establish protections for covered entities' use and disclosure of PHI, it permits use or disclosure in response to certain judicial or administrative orders. Therefore, researchers/contractors may obtain Certificates of Confidentiality to protect them from being forced to disclose information that would have to be disclosed under the Privacy Rule. http://grants.nih.gov/grants/policy/coc/index.htm

IX. Human Subject Regulations Decision Charts

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. 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?

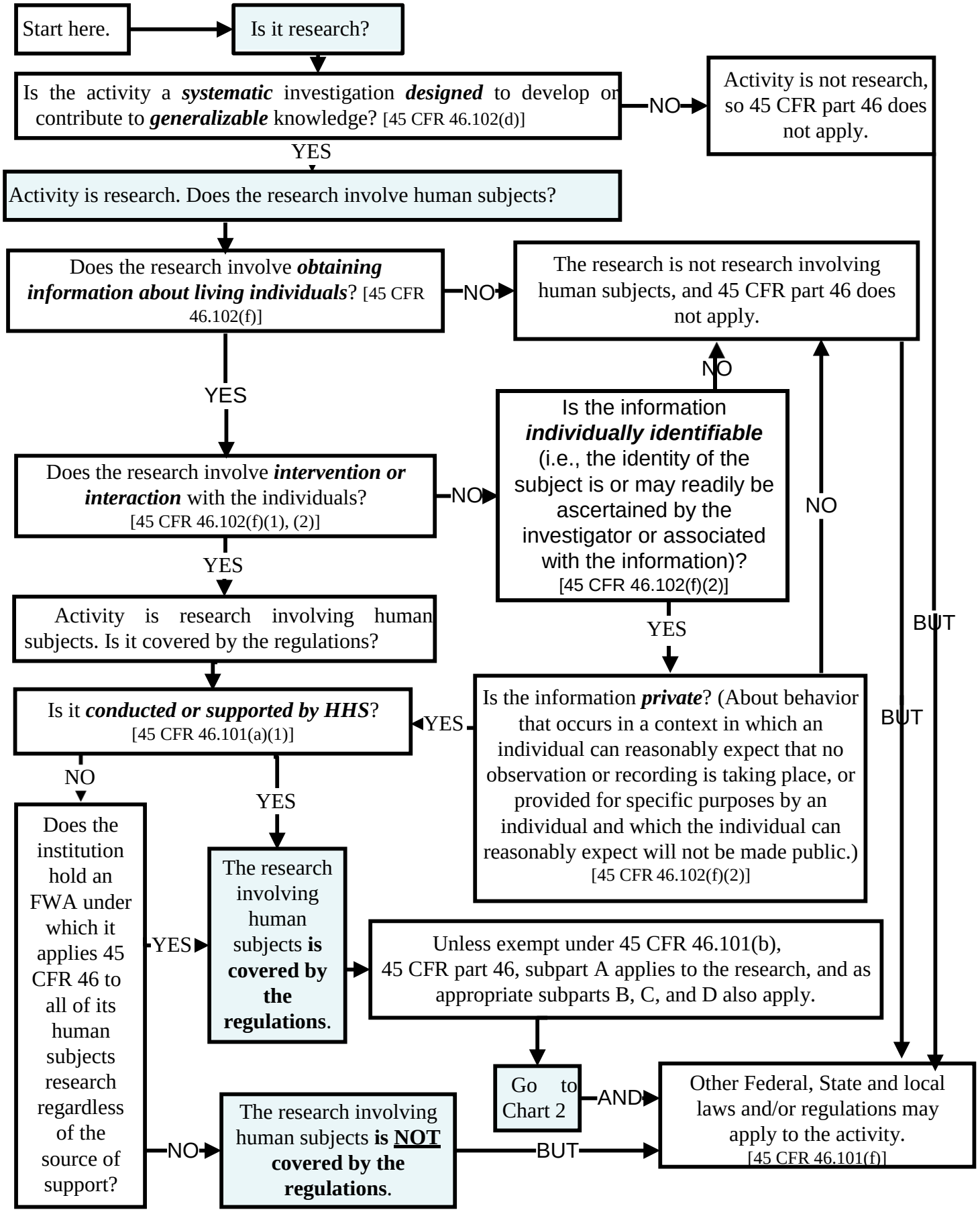


Chart 2: Is the Research Involving Human Subjects Eligible for Exemption Under 45 CFR 46.101(b)?

From Chart 1

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

YES → No exemptions to 45 CFR part 46 apply. Provisions of 45 CFR subpart A apply, and subparts B, C and D also apply if subjects are from covered vulnerable populations. → Go to chart 8

NO

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

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

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

YES → Exemption 45 CFR 46.101(b)(1) may apply. → Go to Chart 3

If not exempt under (b)(1)

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

YES → Exemption 45 CFR 46.101(b)(2) or (b)(3) may apply. → Go to Chart 4

If not exempt under (b)(2) or (b)(3)

Research involving collection or study of ***existing*** data, documents, records, or pathological or diagnostic specimens?

YES → Exemption 45 CFR 46.101(b)(4) may apply. → Go to Chart 5

If not exempt under (b)(4)

Research studying, evaluating, or examining ***public benefit or service programs***?

YES → Exemption 45 CFR 46.101(b)(5) may apply. → Go to Chart 6

If not exempt under (b)(5)

Research involving ***taste and food quality evaluation*** or ***consumer acceptance studies***?

YES → Exemption 45 CFR 46.101(b)(6) may apply. → Go to Chart 7

If not exempt under (b)(6)

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

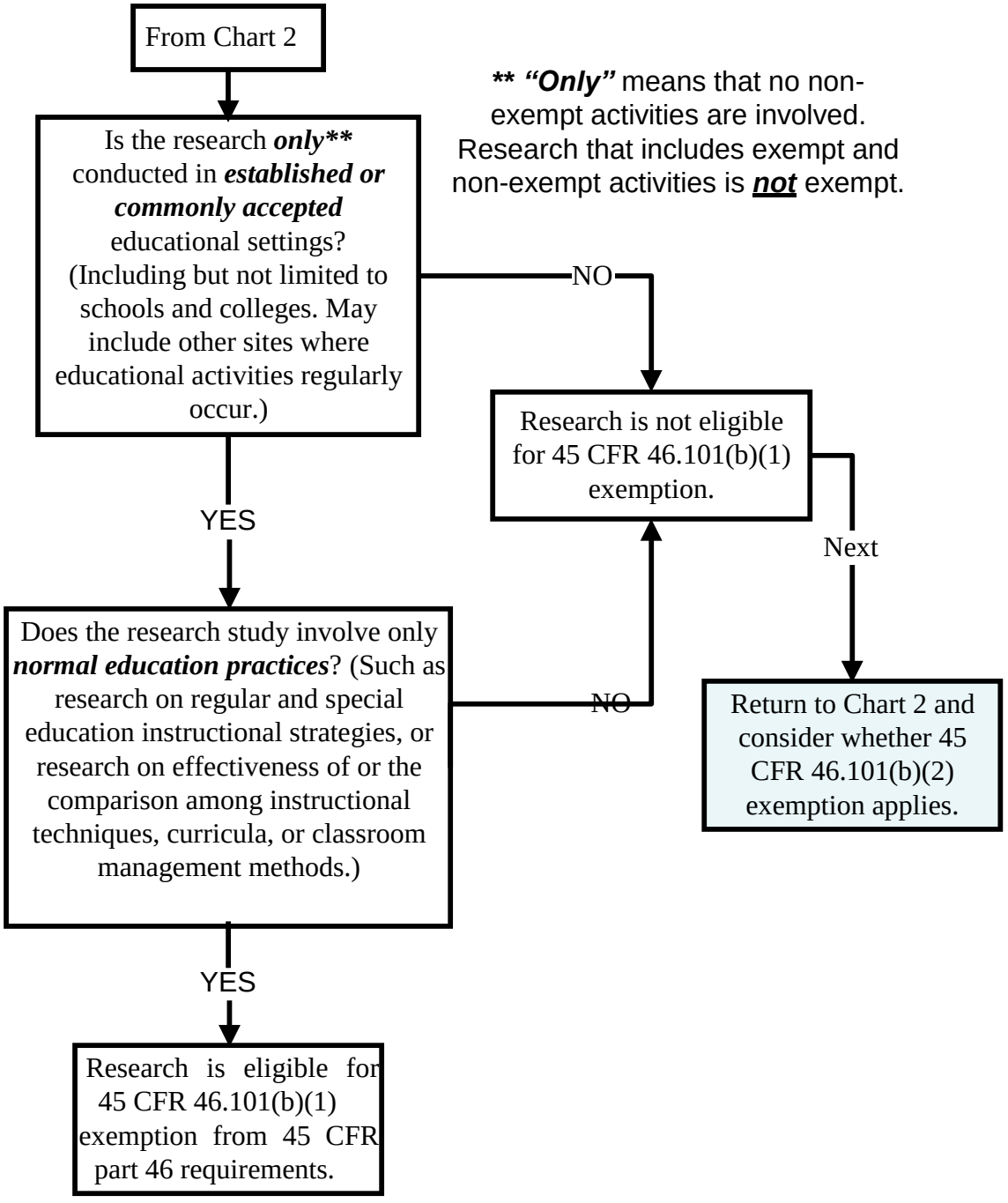


Chart 4: Does Exemption 45 CFR 46.101(b)(2) or (b)(3) (for Tests, Surveys, Interviews, Public Behavior Observation) Apply?

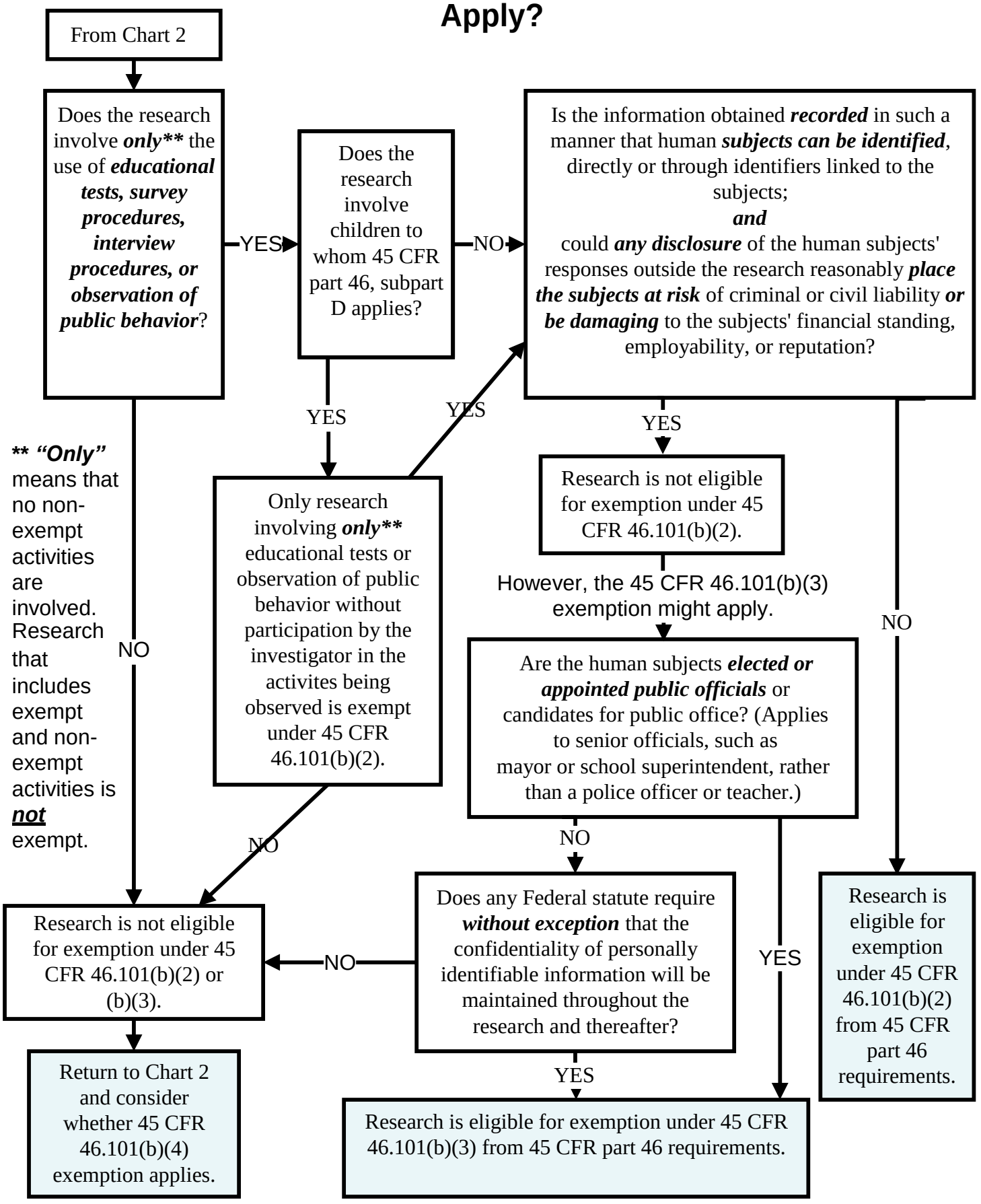
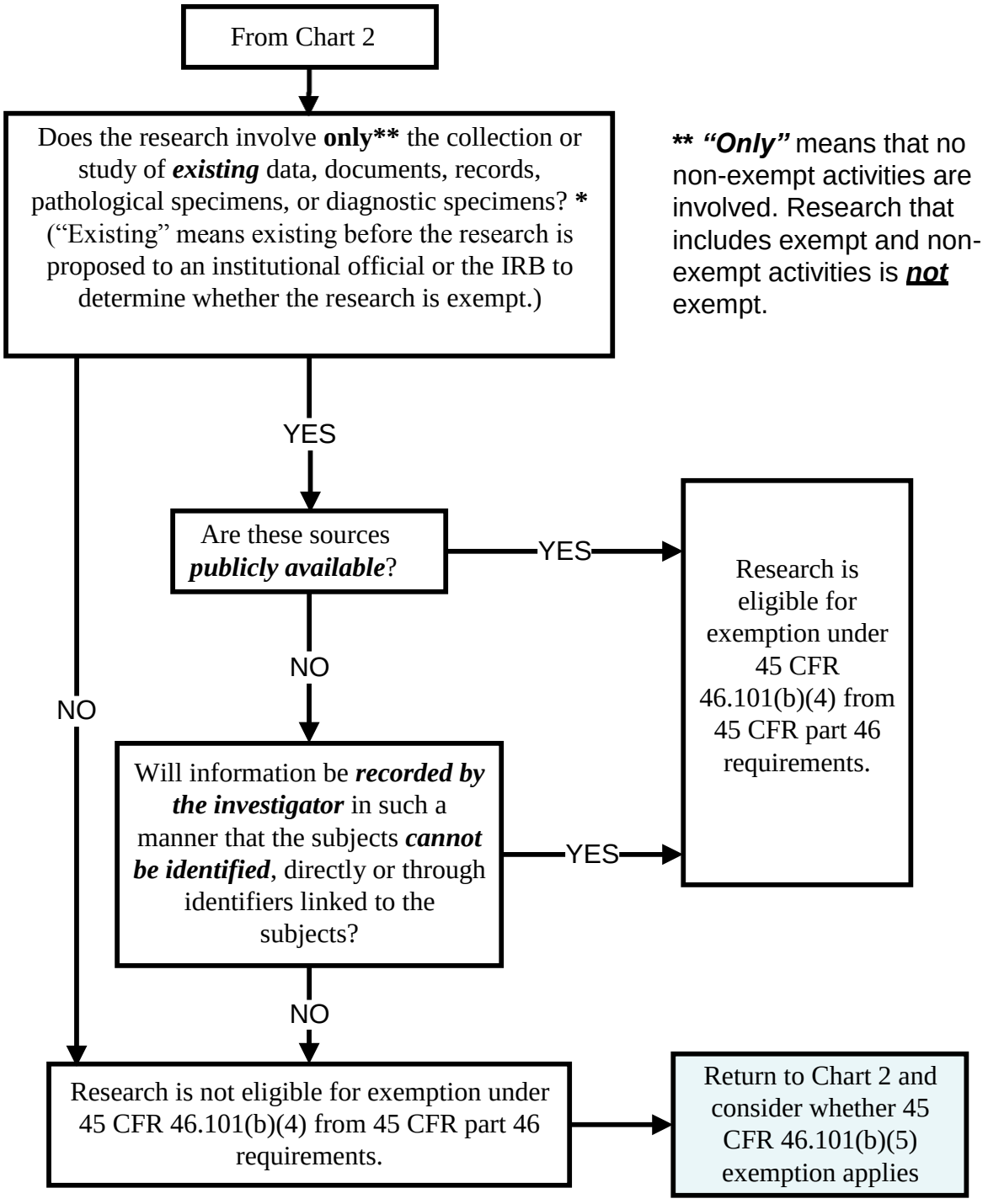
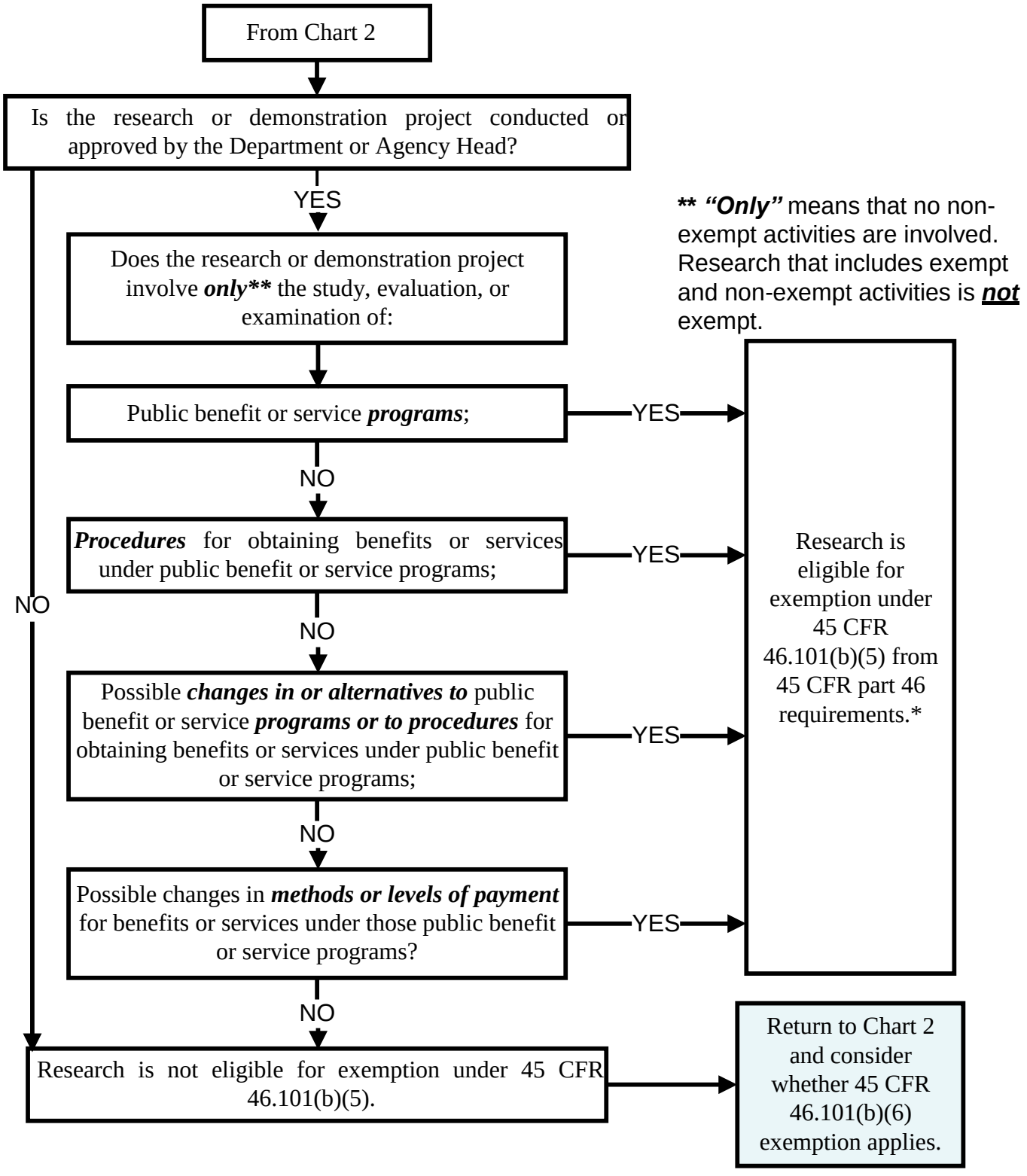


Chart 5: Does Exemption 45 CFR 46.101(b)(4) (for Existing Data Documents and Specimens) Apply?



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

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/regulations-and-policy/guidance/exemptions-for-public-benefit-and-service-programs/index.html for further description of requirements for this exemption.

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

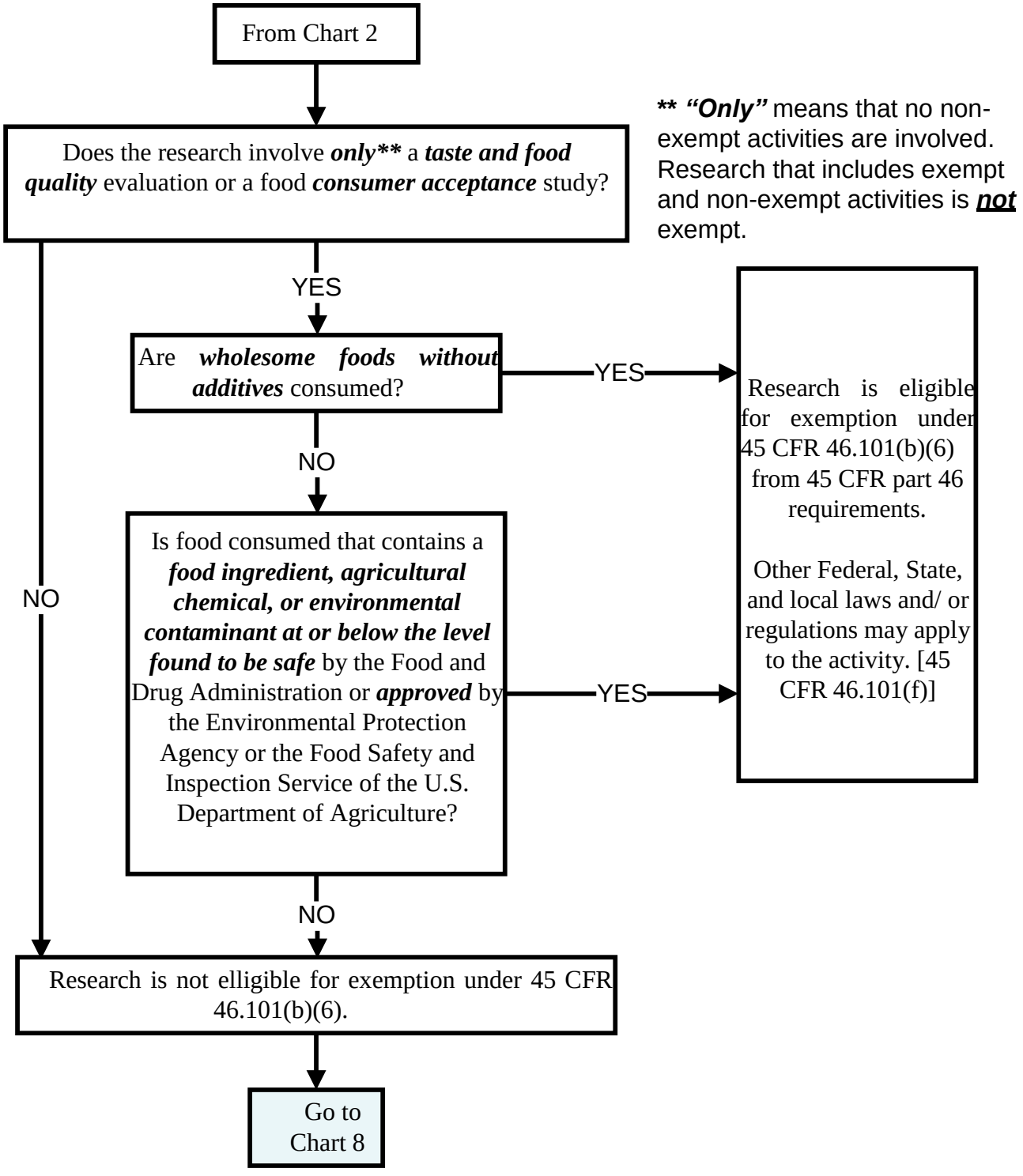


Chart 8: May the IRB Review Be Done by Expedited Procedures Under 45 CFR 46.110?*

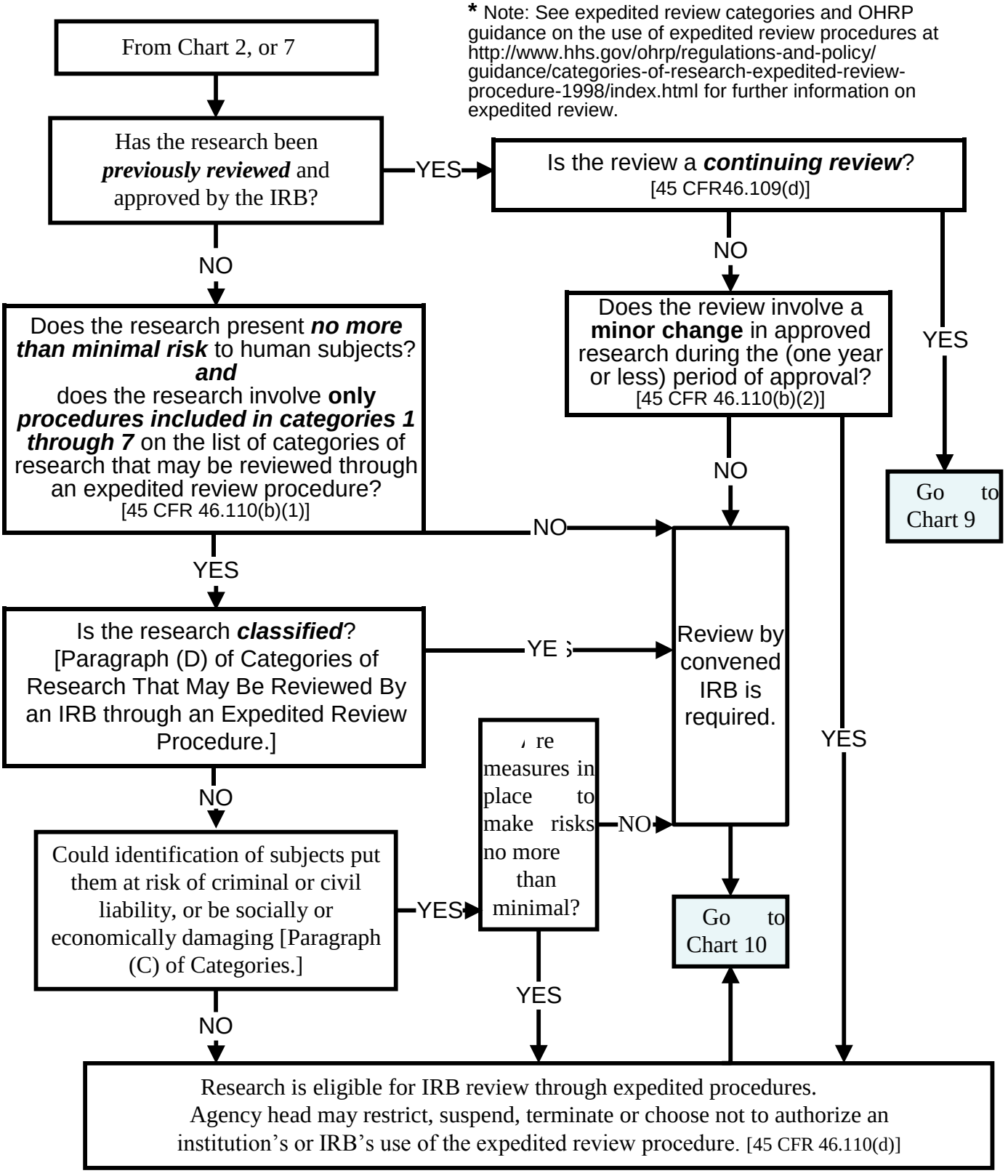


Chart 9: Can Continuing Review be Done by Expedited Procedures Under 45 CFR 46.110?

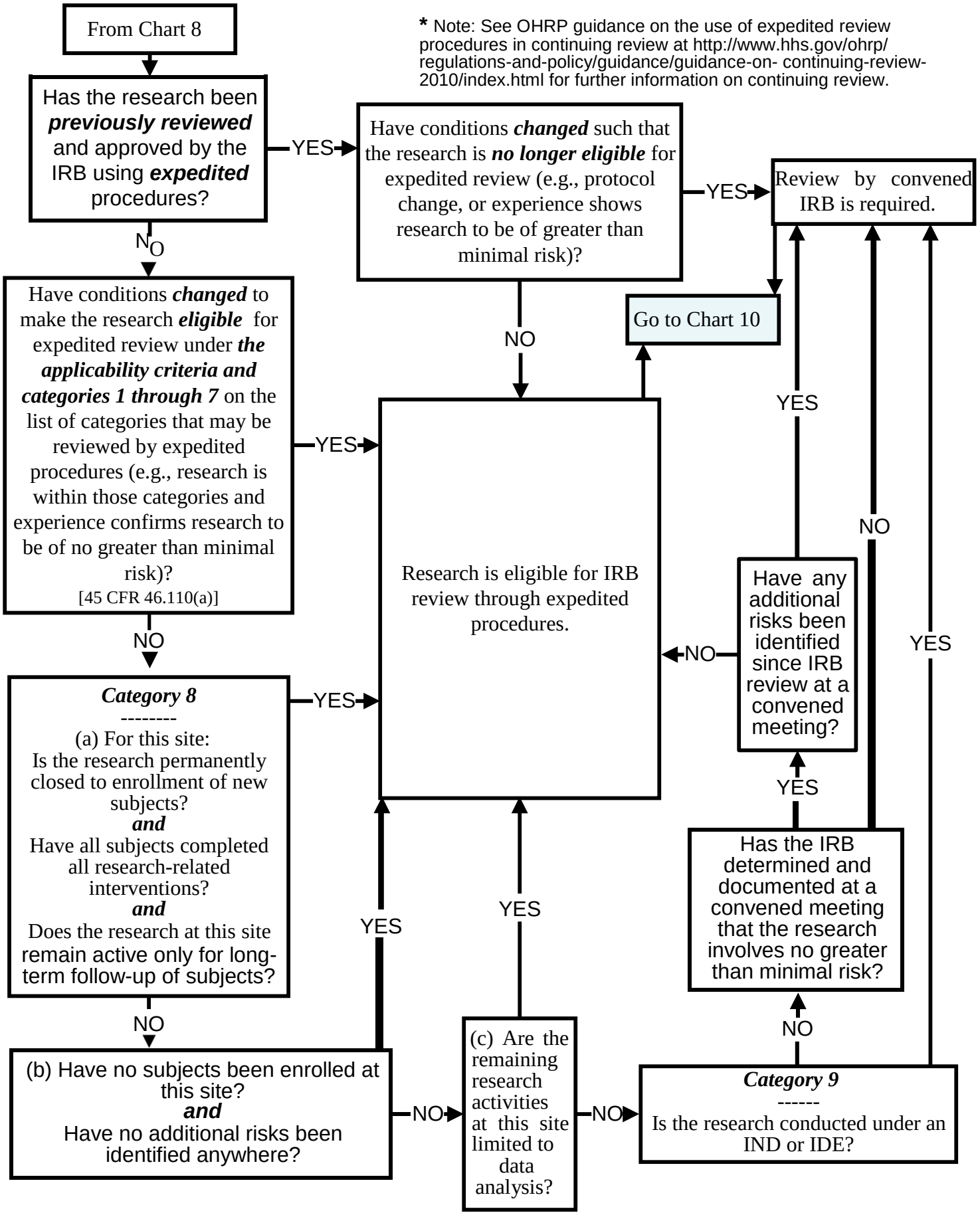
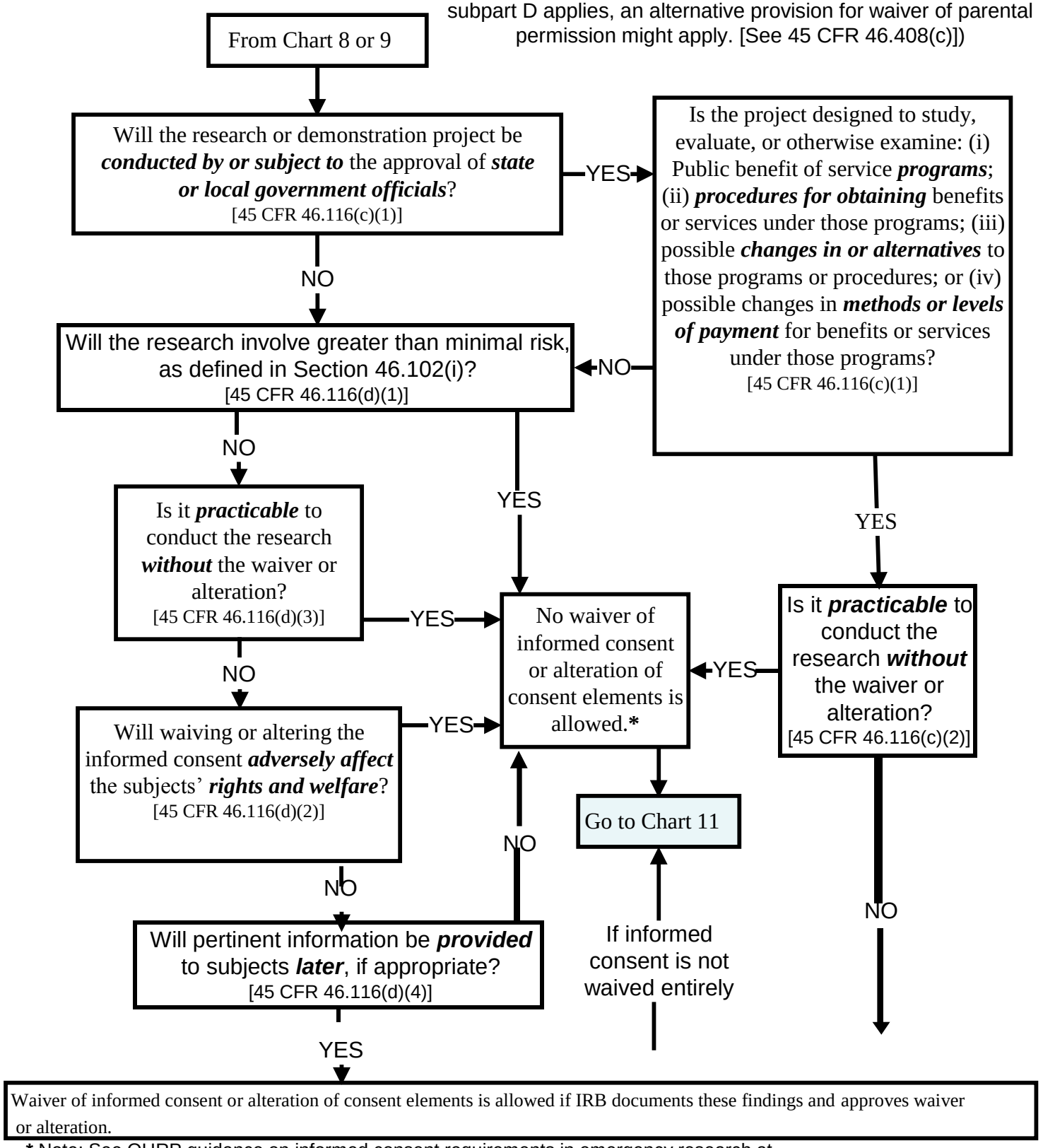


Chart 10: Can Informed Consent Be Waived or Consent Elements Be Altered Under 45 CFR 46.116(c) or (d)?**

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



* Note: See OHRP guidance on informed consent requirements in emergency research at http://www.hhs.gov/ohrp/regulations-and-policy/guidance/emergency-research-informed-consent-requirements/index.html

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