Human Subject Regulations Decision Charts

February 16, 2016

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?

Start here. Is it research?

Is the activity a **systematic** investigation **designed** to develop or contribute to **generalizable** knowledge? [45 CFR 46.102(d)]

- **NO** Activity is not research, so 45 CFR part 46 does not apply.

Activity is research. Does the research involve human subjects?

Does the research involve **obtaining information about living individuals**? [45 CFR 46.102(f)]

- **NO** The research is not research involving human subjects, and 45 CFR part 46 does not apply.

- **YES** Does the research involve **intervention or interaction** with the individuals? [45 CFR 46.102(f)(1), (2)]

  - **NO** Is the information **individually identifiable** (i.e., the identity of the subject is or may readily be ascertained by the investigator or associated with the information)? [45 CFR 46.102(f)(2)]

  - **NO** Is it **conducted or supported by HHS**? [45 CFR 46.101(a)(1)]

    - **NO** Does the institution hold an FWA under which it applies 45 CFR 46 to all of its human subjects research regardless of the source of support?

      - **YES** The research involving human subjects is **covered by the regulations**.

      - **NO** The research involving human subjects is **NOT covered by the regulations**.

    - **YES** The research involving human subjects is **covered by the regulations**.

    - **NO** Go to Chart 2 **AND**

      - **BUT** Other Federal, State and local laws and/or regulations may apply to the activity. [45 CFR 46.101(f)]

      - **BUT** Unless exempt under 45 CFR 46.101(b), 45 CFR part 46, subpart A applies to the research, and as appropriate subparts B, C, and D also apply.

      - **BUT** February 16, 2016
Chart 2: Is the Research Involving Human Subjects Eligible for Exemption Under 45 CFR 46.101(b)?

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

**NO**

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

- Research conducted in established or commonly accepted educational settings, involving normal education practices?
  - YES, Exemption 45 CFR 46.101(b)(1) may apply. Go to Chart 3
  - If not exempt under (b)(1), Exemption 45 CFR 46.101(b)(2) or (b)(3) may apply.

- Research involving the use of educational tests, survey procedures, interview procedures, or observation of public behavior?
  - YES, Exemption 45 CFR 46.101(b)(4) may apply. Go to Chart 4
  - If not exempt under (b)(2) or (b)(3), Exemption 45 CFR 46.101(b)(4) may apply.

- Research involving collection or study of existing data, documents, records, or pathological or diagnostic specimens?
  - YES, Exemption 45 CFR 46.101(b)(5) may apply. Go to Chart 5
  - If not exempt under (b)(4), Exemption 45 CFR 46.101(b)(5) may apply.

- Research studying, evaluating, or examining public benefit or service programs?
  - YES, Exemption 45 CFR 46.101(b)(6) may apply. Go to Chart 6
  - If not exempt under (b)(5), Exemption 45 CFR 46.101(b)(6) may apply.

- 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), 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

**YES**

**“Only”** means that no non-exempt activities are involved. Research that includes exempt and non-exempt activities is **not** exempt.
Chart 3: Does Exemption 45 CFR 46.101(b)(1) (for Educational Settings) Apply?

From Chart 2

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

YES

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

YES

Research is eligible for 45 CFR 46.101(b)(1) exemption from 45 CFR part 46 requirements.

NO

Research is not eligible for 45 CFR 46.101(b)(1) exemption.

NO

Return to Chart 2 and consider whether 45 CFR 46.101(b)(2) exemption applies.

**“Only” means that no non-exempt activities are involved. Research that includes exempt and non-exempt activities is not exempt.
Chart 4: Does Exemption 45 CFR 46.101(b)(2) or (b)(3) (for Tests, Surveys, Interviews, Public Behavior Observation) Apply?

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From Chart 2

Does the research involve only the use of educational tests, survey procedures, interview procedures, or observation of public behavior?

YES

Does the research involve children to whom 45 CFR part 46, subpart D applies?

YES

Only research involving only educational tests or observation of public behavior without participation by the investigator in the activities being observed is exempt under 45 CFR 46.101(b)(2).

NO

Research is not eligible for exemption under 45 CFR 46.101(b)(2) or (b)(3).

RETURN TO CHART 2 AND CONSIDER WHETHER 45 CFR 46.101(b)(4) EXEMPTION APPLIES.

NO

Research is eligible for exemption under 45 CFR 46.101(b)(3) from 45 CFR part 46 requirements.

Does any Federal statute require without exception that the confidentiality of personally identifiable information will be maintained throughout the research and thereafter?

YES

Research is eligible for exemption under 45 CFR 46.101(b)(3) from 45 CFR part 46 requirements.

NO

Research is not eligible for exemption under 45 CFR 46.101(b)(3).

Is the information obtained recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and could any disclosure of the human subjects' responses outside the research reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation?

YES

Research is not eligible for exemption under 45 CFR 46.101(b)(2).

However, the 45 CFR 46.101(b)(3) exemption might apply.

NO

Research is eligible for exemption under 45 CFR 46.101(b)(3) from 45 CFR part 46 requirements.

Are the human subjects elected or appointed public officials or candidates for public office? (Applies to senior officials, such as mayor or school superintendent, rather than a police officer or teacher.)

YES

NO

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

Research is not eligible for exemption under 45 CFR 46.101(b)(2) or (b)(3).
Chart 5: Does Exemption 45 CFR 46.101(b)(4) (for Existing Data Documents and Specimens) Apply?

Does the research involve only** the collection or study of existing data, documents, records, pathological specimens, or diagnostic specimens? *

("Existing" means existing before the research is proposed to an institutional official or the IRB to determine whether the research is exempt.)

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

Are these sources publicly available?

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

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

Research is eligible for exemption under 45 CFR 46.101(b)(4) from 45 CFR part 46 requirements.

Return to Chart 2 and consider whether 45 CFR 46.101(b)(5) exemption applies.

* 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.

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

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

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

YES

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

YES

Public benefit or service programs;

NO

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

NO

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

NO

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

YES

Research is eligible for exemption under 45 CFR 46.101(b)(5) from 45 CFR part 46 requirements.*

NO

Research is not eligible for exemption under 45 CFR 46.101(b)(5).

Return to Chart 2 and consider whether 45 CFR 46.101(b)(6) exemption applies.


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

From Chart 2

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

YES

Are wholesome foods without additives consumed?

YES

Research is eligible for exemption under 45 CFR 46.101(b)(6) from 45 CFR part 46 requirements.

Other Federal, State, and local laws and/or regulations may apply to the activity. [45 CFR 46.101(f)]

NO

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

YES

NO

Research is not eligible for exemption under 45 CFR 46.101(b)(6).

Go to Chart 8

** “Only” means that no non-exempt activities are involved. Research that includes exempt and non-exempt activities is not exempt.
Chart 8: May the IRB Review Be Done by Expedited Procedures Under 45 CFR 46.110?*


From Chart 2, or 7

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

YES

Is the review a continuing review? [45 CFR 46.109(d)]

NO

Does the research present no more than minimal risk to human subjects? and does the research involve only procedures included in categories 1 through 7 on the list of categories of research that may be reviewed through an expedited review procedure? [45 CFR 46.110(b)(1)]

YES

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

NO

Could identification of subjects put them at risk of criminal or civil liability, or be socially or economically damaging [Paragraph (C) of Categories.]

YES

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

NO

Review by convened IRB is required.

YES

Go to Chart 9

NO

NO

Does the review involve a minor change in approved research during the (one year or less) period of approval? [45 CFR 46.110(b)(2)]

NO

Go to Chart 10

YES

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

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

From Chart 8

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

YES

Go to Chart 10

NO

Have conditions changed to make the research eligible for expedited review under the applicability criteria and categories 1 through 7 on the list of categories that may be reviewed by expedited procedures (e.g., research is within those categories and experience confirms research to be of no greater than minimal risk)?

[45 CFR 46.110(a)]

NO

Research is eligible for IRB review through expedited procedures.

YES

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

Review by convened IRB is required.

NO

Go to Chart 10

Category 8

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

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

NO

YES

NO

YES

Category 9

Is the research conducted under an IND or IDE?

NO

YES

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

NO

YES

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

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NO

YES

(c) Are the remaining research activities at this site limited to data analysis?

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

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

From Chart 8 or 9

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

YES

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

YES

Go to Chart 11

NO

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

NO

Will it be practicable to conduct the research without the waiver or alteration? [45 CFR 46.116(d)(3)]

YES

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

NO

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

YES

Is it practicable to conduct the research without the waiver or alteration? [45 CFR 46.116(c)(2)]

YES

If informed consent is not waived entirely

NO

Go to Chart 11

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

YES

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

NO

* 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 for further information on emergency research informed consent waiver.
Chart 11: May Documentation of Informed Consent Be Waived Under 45 CFR 46.117(c)?

From Chart 10

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

NO

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

YES

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

NO

IRB may NOT waive the requirement for a signed consent form for any subjects.

YES

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

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

AND

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

AND

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

END

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