SCOPE: The following graphic charts are intended to aid those who need to decide if an activity is research involving human subjects that must be reviewed by an institutional review board (IRB) and whether informed consent or the documentation of informed consent can be waived under the 2018 Requirements found for the U.S. Department of Health and Human Services (HHS) at 45 CFR part 46, Subpart A.

TARGET AUDIENCE: IRBs, institutions, investigators, and others

CONSIDERATIONS: These charts are necessarily generalizations and may not be specific enough for particular situations. Other guidance documents are available related to specific topics at https://www.hhs.gov/ohrp/regulations-and-policy/guidance/index.html. OHRP cautions that the full text of an applicable regulatory provision should be considered in making final decisions. The charts do not address requirements that may be imposed by other organizations, such as the Food and Drug Administration, the National Institutes of Health, other sponsors, or state or local governments.

CHART 01: IS AN ACTIVITY HUMAN SUBJECTS RESEARCH COVERED BY 45 CFR PART 46?
CHART 02: IS THE RESEARCH INVOLVING HUMAN SUBJECTS ELIGIBLE FOR EXEMPTION UNDER 45 CFR 46.104(d)?
CHART 03: DOES EXEMPTION 45 CFR 46.104(d)(1) FOR EDUCATIONAL PRACTICES APPLY?
CHART 04: DOES EXEMPTION 45 CFR 46.104(d)(2) FOR EDUCATIONAL TESTS, SURVEYS, INTERVIEWS, OR OBSERVATION OF PUBLIC BEHAVIOR APPLY?
CHART 05: DOES EXEMPTION 45 CFR 46.104(d)(3) FOR BENIGN BEHAVIORAL INTERVENTIONS APPLY?
CHART 06: DOES EXEMPTION 45 CFR 46.104(d)(4) FOR SECONDARY RESEARCH THAT DOES NOT REQUIRE CONSENT APPLY?
CHART 07: DOES EXEMPTION 45 CFR 46.104(d)(5) FOR PUBLIC BENEFIT OR SERVICE PROGRAMS APPLY?
CHART 08: DOES EXEMPTION 45 CFR 46.104(d)(6) FOR FOOD, TASTE, AND ACCEPTANCE STUDIES APPLY?
CHART 09: DOES EXEMPTION 45 CFR 46.104(d)(7), STORAGE FOR SECONDARY RESEARCH FOR WHICH BROAD CONSENT IS REQUIRED, APPLY?
CHART 10: DOES EXEMPTION 45 CFR 46.104(d)(8) FOR SECONDARY RESEARCH FOR WHICH BROAD CONSENT IS REQUIRED APPLY?
CHART 11: IS CONTINUING REVIEW REQUIRED UNDER 45 CFR 46.109(f)?
CHART 12: WAIVER OR ALTERATION OF INFORMED CONSENT IN RESEARCH INVOLVING PUBLIC BENEFIT AND SERVICE PROGRAMS CONDUCTED BY OR SUBJECT TO THE APPROVAL OF STATE OR LOCAL GOVERNMENT OFFICIALS (45 CFR 46.116(e))
CHART 13: WHEN CAN INFORMED CONSENT BE WAIVED OR ALTERED UNDER 45 CFR 46.116(f)?
CHART 14: CAN DOCUMENTATION OF INFORMED CONSENT BE WAIVED UNDER 45 CFR 46.117(c)?
CHART 01
IS AN ACTIVITY HUMAN SUBJECTS RESEARCH COVERED BY 45 CFR PART 46?
NOTE: This chart is consistent with the 2018 Requirements (i.e., the revised Common Rule)

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Is the activity a systematic investigation designed to develop or contribute to generalizable knowledge?

[45 CFR 46.102(l)]

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

Yes
  - Does the activity fit the criteria for excluded research at 45 CFR 46.102(l)(1)-(4)?
    - No
      - Activity is research.
    - Yes
      - Does the research involve a living individual about whom an investigator conducting research obtains information or biospecimens through intervention or interaction with the individual and uses, studies, or analyzes the information or biospecimens?
        - No
          - The activity is not research involving human subjects and 45 CFR part 46 does not apply.
        - Yes
          - Does the research involve a living individual about whom an investigator conducting research obtains, uses, studies, analyzes, or generates identifiable private information or identifiable biospecimens?
            - No
              - The research involving human subjects is covered by the regulations.
            - Yes
              - 45 CFR part 46, subpart A applies to the research, and as appropriate, subparts B, C, D, and E also apply.

Is the research involving human subjects conducted or supported by HHS?

- Yes
  - The research involving human subjects is covered by the regulations.
- No
  - The research involving human subjects is NOT covered by the HHS regulations. Institutions may choose to follow regulatory procedures even when not required to do so.*

*For information on whether an institution needs to revise its FWA because of the 2018 Requirements, see, https://www.hhs.gov/ohrp/education-and-outreach/revised-common-rule/revised-common-rule-q-and-a/index.html
IS THE RESEARCH INVOLVING HUMAN SUBJECTS ELIGIBLE FOR EXEMPTION UNDER 45 CFR 46.104(d)?

NOTE: This chart is consistent with the 2018 Requirements (i.e., the revised Common Rule)

For use after January 20, 2019

Has HHS prohibits exemption of the human subjects research? (Most research involving prisoners, some research involving children.)

- Yes → No exemptions to 45 CFR part 46 apply. Provisions of 45 CFR part 46, subpart A apply, and subparts B, C, and D also apply if subjects are members of populations covered in those subparts.

- 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 46.104(d)(1) may apply. Go to Chart 03
  - No → Exemption 45 CFR 46.104(d)(2) may apply. Go to Chart 04

- Research only including interactions involving educational tests, survey procedures, interview procedures, or observation of public behavior?
  - Yes → Exemption 45 CFR 46.104(d)(3) may apply. Go to Chart 05
  - No → Exemption 45 CFR 46.104(d)(4) or (d)(8) may apply. Go to Chart 06 & Chart 10

- Research involving benign behavioral interventions and collection of information from adults with their agreement?
  - Yes → Exemption 45 CFR 46.104(d)(5) may apply. Go to Chart 07
  - No → Exemption 45 CFR 46.104(d)(6) may apply. Go to Chart 08

- Secondary research use of identifiable private information or identifiable biospecimens?
  - Yes → Exemption 45 CFR 46.104(d)(7) may apply. Go to Chart 09
  - No → Exemption 45 CFR 46.104(d)(7) may apply.

- Research studying, evaluating, or examining public benefit or service programs?
  - Yes → Exemption 45 CFR 46.104(d)(8) may apply. Go to Chart 07
  - No → Exemption 45 CFR 46.104(d)(7) may apply.

- Research involving taste and food quality evaluation of consumer acceptance studies?
  - Yes → Exemption 45 CFR 46.104(d)(7) may apply. Go to Chart 09
  - No → Exemption 45 CFR 46.104(d)(7) may apply.

- Storage or maintenance of identifiable private information or identifiable biospecimens for secondary research use?
  - Yes → Exemption 45 CFR 46.104(d)(7) may apply. Go to Chart 09
  - No → Exemption 45 CFR 46.104(d)(7) may apply.

*Only means that no nonexempt activities are involved. Research that excludes both exempt and nonexempt activities is not exempt. Research may involve activities exempt under more than one exemption category.
Does Exemption 45 CFR 46.104(d)(1) for Educational Practices Apply?

**NOTE:** This chart is consistent with the 2018 Requirements (i.e., the revised Common Rule)

TO BE EXEMPT, NO NONEXEMPT ACTIVITIES CAN BE INVOLVED. RESEARCH THAT INCLUDES BOTH EXEMPT AND NONEXEMPT ACTIVITIES IS NOT EXEMPT. RESEARCH MAY INVOLVE ACTIVITIES EXEMPT UNDER MORE THAN ONE EXEMPTION CATEGORY.

1. **Start Here**
2. Is the research conducted in established or commonly accepted educational settings?
   - **Yes**
     - Does the research specifically involve normal education practices not likely to adversely impact students’ opportunity to learn required educational content or assessment of educators who provide instruction? This includes most research on regular and special education instructional strategies, instructional techniques, curricula, or classroom management methods.
       - **Yes**
         - Research may be exempt under 45 CFR 46.104(d)(1).
       - **No**
         - Research is not exempt under 45 CFR 46.104(d)(1) exemption. Go to the other exemption decision charts to see if any other exemptions apply.
   - **No**
     - Research is not exempt under 45 CFR 46.104(d)(1) exemption. Go to the other exemption decision charts to see if any other exemptions apply.
Does the research only include interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), survey procedures, interview procedures, or observation of public behavior (including visual or auditory recordings)?

No

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

Yes

The exemption may apply. However, when the subjects are children, this may only apply to research involving educational tests or the observation of public behavior when the investigator does not participate in the activities being observed.

Or

Is it the case that any disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation?

Yes

The exemption may apply unless the research involves children. This condition does not apply to research subject to Subpart D.

Or

Is the information obtained recorded by the investigator in such a manner that the identity of the human subjects can readily be ascertained, directly or through identifiers linked to the subjects, and has an IRB conducted a limited review to make the determination required by 45 CFR 46.111(a)(7)?

No

Yes

The research is not exempt under 45 CFR 46.104(d)(2). Go to the other exemption decision charts to see if any other exemptions apply.
Does the research involve benign behavioral interventions* in conjunction with collection of information from adults through verbal or written responses (including data entry) or audiovisual recording?

- Yes
  - Have the subjects prospectively agreed to the intervention and information collection?
    - Yes
      - Is the information obtained recorded in such a manner that human subjects can be readily identified, directly or through identifiers linked to the subjects?
        - Yes
          - Has an IRB conducted a limited review to make the determinations required by 45 CFR 46.111(a)(7); that, when appropriate, there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data?
            - Yes
              - Research may be exempt under 45 CFR 46.104(d)(3).
            - No
              - No

- No
  - The research is not exempt under 45 CFR 46.104(d)(3).
    - Go to the other exemption decision charts to see if any other exemptions apply.

- No
  - 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, educational advancement, or reputation?
    - Yes
      - Exemption 45 CFR 46.104(d)(3) does not apply if the research involves deceiving subjects regarding the nature or purposes of the research unless the subject authorizes the deception through prospective agreement to be unaware of or misled regarding the nature or purposes of the research.
    - No
      - Research may be exempt under 45 CFR 46.104(d)(3).

*Benign behavioral interventions are brief in duration, harmless, painless, not physically invasive, not likely to have a significant adverse lasting impact on the subjects, and the investigator has no reason to think the subjects will find the interventions offensive or embarrassing.
TO BE EXEMPT, NO NONEXEMPT ACTIVITIES CAN BE INVOLVED. RESEARCH THAT INCLUDES BOTH EXEMPT AND NONEXEMPT ACTIVITIES IS NOT EXEMPT. RESEARCH MAY INVOLVE ACTIVITIES EXEMPT UNDER MORE THAN ONE EXEMPTION CATEGORY.

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Does the research involve **secondary uses** of identifiable private information or identifiable biospecimens? *

- **Yes**
  - The research is not exempt under 45 CFR 46.104(d)(4).
  - Go to the other exemption decision charts to see if any other exemptions apply.

- **No**
  - Is the identifiable private information or are the identifiable biospecimens publicly available? [45 CFR 46.104(d)(4)(i)]
    - **Yes**
      - Research may be exempt under 45 CFR 46.104(d)(4).
    - **Or**
      - Is the information, which may include information about biospecimens, recorded by the investigator in such a manner that the identity of the human subjects cannot readily be ascertained directly or through identifiers linked to the subjects, the investigator does not contact the subjects, and the investigator will not re-identify subjects? [45 CFR 46.104(d)(4)(ii)]
        - **Yes**
          - Is the research conducted or supported by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch activities, and the research generates identifiable private information that is or will be maintained on information technology subject to and in compliance with section 208(b) of the E-Government Act of 2002, and all of the identifiable private information collected, used, or generated as part of the activity will be maintained in systems of records subject to the Privacy Act of 1974, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995? [45 CFR 46.104(d)(4)(iv)]
            - **Yes**
              - Research may be exempt under 45 CFR 46.104(d)(4).
            - **Or**
              - Does the research involve only information collection and analysis involving the investigator’s use of identifiable health information when that use is regulated under 45 CFR parts 160 and 164, subparts A and E, for purposes of “healthcare operations” or “research” as defined at 45 CFR 164.501 or for “public health activities and purposes” as described under 45 CFR 164.512(b)? [45 CFR 46.104(d)(4)(iii)]
                - **Yes**
                  - Research may be exempt under 45 CFR 46.104(d)(4).
                - **Or**
                  - Does the research use of identifiable private information or identifiable biospecimens collected for either research studies other than the proposed research, or for nonresearch purposes.

*Research use of identifiable private information or identifiable biospecimens collected for either research studies other than the proposed research, or for nonresearch purposes.*
TO BE EXEMPT, NO NONEXEMPT ACTIVITIES CAN BE INVOLVED. RESEARCH THAT INCLUDES BOTH EXEMPT AND NONEXEMPT ACTIVITIES IS NOT EXEMPT. RESEARCH MAY INVOLVE ACTIVITIES EXEMPT UNDER MORE THAN ONE EXEMPTION CATEGORY.

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Is the research or demonstration project conducted or supported by a Federal department or agency or otherwise subject to approval by the conducting or supporting department or agency’s head or delegate?

No

Research is not exempt under 45 CFR 46.104(d)(5). Go to the other exemption decision charts to see if any other exemptions apply.

Yes

Is the research or demonstration project designed to study, evaluate, improve, or otherwise examine public benefit or service programs, including:

- Procedures for obtaining benefits or services under those programs;
- Possible changes in or alternatives to those programs or procedures; or
- Possible changes in methods or levels of payment for benefits or services under those public benefit or service programs?

No

Research may be exempt under 45 CFR 46.104(d)(5).

Yes

The Federal department or agency must publish a list of projects conducted or supported under this provision prior to starting the research.
ChART 08

DOES EXEMPTION 45 CFR 46.104(d)(6) FOR FOOD, TASTE, AND ACCEPTANCE STUDIES APPLY?

NOTE: This chart is consistent with the 2018 Requirements (i.e., the revised Common Rule)

TO BE EXEMPT, NO NONEXEMPT ACTIVITIES CAN BE INVOLVED. RESEARCH THAT INCLUDES BOTH EXEMPT AND NONEXEMPT ACTIVITIES IS NOT EXEMPT. RESEARCH MAY INVOLVE ACTIVITIES EXEMPT UNDER MORE THAN ONE EXEMPTION CATEGORY.

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

- Yes
  - Are wholesome foods without additives consumed?
    - Yes
      - Research may be exempt under 45 CFR 46.104(d)(6).
    - Or
      - Is a food 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?
        - Yes
          - Research may be exempt under 45 CFR 46.104(d)(6).
        - No
          - Research is not exempt under 45 CFR 46.104(d)(6). Go to the other exemption decision charts to see if any other exemptions apply.
  - No

- No
  - Research is not exempt under 45 CFR 46.104(d)(6). Go to the other exemption decision charts to see if any other exemptions apply.
Does the research involve storage or maintenance of identifiable private information or identifiable biospecimens for potential secondary research?*

- **Yes**
  - Has an IRB conducted a limited review and made the determinations required by 45 CFR 46.111(a)(8) that:
    - Broad consent for storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens is obtained in accordance with 45 CFR 46.116(a)(1)-(4), (a)(6), and (d);
    - Broad consent is appropriately documented or waiver of documentation is appropriate, in accordance with 45 CFR 46.117;
    - If a change is made for research purposes in the way the identifiable private information or identifiable biospecimens are stored or maintained, there are adequate provisions to protect the privacy of subjects and maintain the confidentiality of data?
      - **Yes**
        - Research may be exempt under 45 CFR 46.104(d)(7).
      - **No**
        - Research is not exempt under 45 CFR 46.104(d)(7). Go to the other exemption decision charts to see if any other exemptions apply.

- **No**
  - Secondary research involving storage or maintenance of private information or biospecimens that are not identifiable does not involve human subjects and 45 CFR part 46 does not apply.

*Research use of identifiable private information or identifiable biospecimens collected for either research studies other than the proposed research, or for nonresearch purposes.
TO BE EXEMPT, NO NONEXEMPT ACTIVITIES CAN BE INVOLVED. RESEARCH THAT INCLUDES BOTH EXEMPT AND NONEXEMPT ACTIVITIES IS NOT EXEMPT. RESEARCH MAY INVOLVE ACTIVITIES EXEMPT UNDER MORE THAN ONE EXEMPTION CATEGORY.

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Does the research involve use of identifiable private information or identifiable biospecimens for secondary research?*

Yes
Was broad consent for storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens obtained in accordance with 45 CFR 46.116(a)(1)-(4), (a)(6), and (d)?

Yes
Was documentation of informed consent obtained, or was documentation of informed consent appropriately waived in accordance with 45 CFR 46.117?

Yes
Has an IRB conducted a limited review and made the determination required by 45 CFR 46.111(a)(7) and determined that the research is within the scope of the broad consent referenced in 45 CFR 46.104(d)(8)(i)?

Yes
Does the investigator include returning individual research results to subjects in the study plan?

Yes
Research may be exempt under 45 CFR 46.104(d)(8).

No
Research is not exempt under 45 CFR 46.104(d)(8).

No
Go to the other exemption decision charts to see if any other exemptions apply.

No
Research use of identifiable private information or identifiable biospecimens collected for either research studies other than the proposed research, or for nonresearch purposes.

*Research use of identifiable private information or identifiable biospecimens collected for either research studies other than the proposed research, or for nonresearch purposes.
Is the research eligible for expedited review in accordance with 45 CFR 46.110?

Yes

Was the prior IRB review a limited review conducted as part of an exemption determination under 45 CFR 46.104(d)?

Yes

Has the research progressed to the point that it involves only data analysis (including analysis of identifiable private information or identifiable biospecimens), which is part of the IRB-approved study?

Yes

Has the research progressed to the point that it involves only accessing follow-up clinical data from procedures subjects would undergo as part of clinical care, which is part of the IRB-approved study?

Yes

No

Continuing review is required.

NOTE: This chart is consistent with the 2018 Requirements (i.e., the revised Common Rule)
WAIVER OR ALTERATION OF INFORMED CONSENT IN RESEARCH INVOLVING PUBLIC BENEFIT AND SERVICE PROGRAMS CONDUCTED BY OR SUBJECT TO THE APPROVAL OF STATE OR LOCAL GOVERNMENT OFFICIALS (45 CFR 46.116(e))

NOTE: This chart is consistent with the 2018 Requirements (i.e., the revised Common Rule) For use after January 20, 2019

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Has an IRB found and documented that the research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine any of the following:

- Public benefit or service programs;
- Procedures for obtaining benefits or services under those programs;
- Possible changes in or alternatives to those programs or procedures; or
- Possible changes in methods or levels of payment for benefits or services under those programs?

[45 CFR 46.116(e)(3)(i)]

No

No waiver or alteration of informed consent is allowed.

Yes

Has an IRB found and documented that the research could not practicably be carried out without the waiver or alteration?

[45 CFR 46.116(e)(3)(ii)]

No

Waiver: An IRB may waive the requirement to obtain informed consent, provided the IRB satisfies the requirements for waiver at 45 CFR 46.116(e). However, if an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at 45 CFR 46.116(d), and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

[45 CFR 46.116(e)(1)]

Or

Alteration: An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent found at 45 CFR 46.116(b) and (c) provided the IRB satisfies the requirements at 45 CFR 46.116(e). However, an IRB may not omit or alter any of the requirements described at 45 CFR 46.116(a). If a broad consent procedure is used, an IRB may not omit or alter any of the elements required at 45 CFR 46.116(d) as stipulated under 45 CFR 46.116(e)(2).

[45 CFR 46.116(e)(2),(3)]
Has an IRB found and documented that all of the following conditions have been met?

- The research involves no more than minimal risk to the subjects;
- The research could not practicably be carried out without the requested waiver or alteration;
- If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;
- The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
- Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

No waiver or alteration of informed consent is allowed.

Waiver: An IRB may waive the requirement to obtain informed consent for research provided the IRB satisfies this requirement. However, if an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at 45 CFR 46.116(d), and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

Alteration: An IRB may approve a consent procedure that omits some, or alters some or all, of the elements of informed consent set forth in 45 CFR 46.116(b) and (c) provided the IRB satisfies this requirement. However, an IRB may not omit or alter any of the requirements described at 45 CFR 46.116(a). If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under 45 CFR 46.116(d).
CAN DOCUMENTATION OF INFORMED CONSENT BE WAIVED UNDER 45 CFR 46.117(c)?

NOTE: This chart is consistent with the 2018 Requirements (i.e., the revised Common Rule) for use after January 20, 2019.

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Has an IRB found any of the following?

That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Further, each subject (or legally authorized representative) will be asked whether the subject wants documentation linking the subject with the research, and the subject’s wishes will govern.

[45 CFR 46.117(c)(1)(i)]

Yes:

An IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects or legally authorized representatives with a written statement regarding the research.

Or

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

[45 CFR 46.117(c)(1)(ii)]

Yes:

Or

If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained.

[45 CFR 46.117(c)(1)(iii)]

Yes:

No:

Documentation of informed consent cannot be waived. See 45 CFR 46.117(b) to assess what form the documentation might take.