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Determinations of Research, Human Subjects Research, Exemptions, and Expedited Review

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Key Questions
Ask in the Following Order

Answer questions in proper sequence when determining whether an activity is research, human subjects research, exempt, or can be expedited.

1. Is this project **research**?
2. If so, does it involve **human subjects**?
3. If so, is it **exempt**?
4. If it is not exempt, is it eligible for ***expedited*** review?

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Is this project **Research**?

Common Rule Definition of **Research:**

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

38 CFR 16.102(d)

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Key Terms*

- A ***systematic investigation*** is a project that is planned in advance and that uses data collection and analysis to answer a question.

- ***Generalizable knowledge*** is information that expands scientific understanding or the knowledge base of a scholarly field of study.

*ORO Presentation on VHA Operations Activities That May Constitute Research (6/18/2010)

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Project is Not Research if:*

- Designed solely for VA's **internal** purposes, and
- Is **not** designed to be generalized beyond VA (i.e. **not** designed to expand scientific understanding or knowledge of base of a scholarly field of study.)

*ORO Presentation on VHA Operations Activities That May Constitute Research (6/18/2010)

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Project is Always Research if it is:*

- Funded or supported as research, or
- Clinical Investigation as defined by FDA.

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Design Characteristics Warranting Particular Attention*

The following design characteristics are often employed to generate findings that are generalizable. Inclusion of one or more of these characteristics in a health care or other operations activity warrants particular attention in determining whether the activity constitutes research:

- Randomization of individuals;
- Randomization of service units;
- Stratification;
- Matched pairs;

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Design Characteristics Warranting Particular Attention* (Continued)

- Double blinding;
- Use of placebo;
- Assessment of an intervention that is not yet standard or accepted practice;
- Comparison of two more interventions;
- Collection of clinical information that is not medically necessary;
- An intervention that is not designed for the benefit of the patient;
- Use of identifiable patient or employee survey data.

*ORO Presentation on VHA Operations Activities That May Constitute Research (6/18/2010)

If Research, does it involve Human Subjects?

Common Rule Definition of **Human Subject:**

Human subject means a living individual **about whom** an investigator conducting research obtains:

- data through intervention or interaction with the individual, or
- identifiable private information.

38 CFR 16.102(f)

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If Research, does it involve Human Subjects?

Common Rule Definition of **Human Subject** (continued):

- An ***intervention*** includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes.
- ***Interaction*** includes communication or interpersonal contact between investigator and subject.

38 CFR 16.102(f)

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If Research, does it involve Human Subjects?

Common Rule Definition of **Human Subject** (continued):

- ***Private information*** includes information about:
  - behavior in which an individual can reasonably expect that no observation or recording is taking place, and
  - information provided for specific purposes which the individual can reasonably expect will not be made public (e.g., medical record)
- ***Private information*** must be ***individually identifiable*** to constitute research involving human subjects (identity of the subject is or may readily be ascertained by the investigator or associated with the information.)

38 CFR 16.102(f)

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Questions to Determine if Research Involves Human Subjects*

- Does the research involve obtaining information about living individuals?
- Does the research involve an intervention or interaction with the individuals?
- Is the information individually identifiable?
- Is the information private?

*OHRP Human Subject Regulations Decision Charts

Decision Charts (9/24/2004)

www.hhs.gov/ohrp/humansubjects/guidance/decisioncharts.htm

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Private Information/Specimens Are Not Individually Identifiable If ...*

- …they are not collected specifically for the currently proposed research;

-AND-

- Investigators cannot *readily* ascertain the identity of the individuals to whom the coded private information/specimens pertain because of prohibitions to release of the key to the code (e.g., agreement, IRB-approved policy, legal requirements.)

*OHRP Guidance Coded Private Information or Biological Specimens (10/16/2008)

www.hhs.gov/ohrp/humansubjects/guidance/cdebiol.htm

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If it is human subjects research, is it **exempt**?

- Research activities in which the only involvement of human subjects will be in one or more of the categories outlined in 38 CFR 16.101(b) may be exempt from the provisions of the Common Rule (Title 38 CFR part 16.)
- Investigator must submit proposed research study and request for exemption to the IRB.
- The IRB Chair, or experienced IRB voting member designated by the Chair, determines whether to grant exemption and records the determination.

NOTE: VHA Handbooks 1200.01 & 1200.05 apply to all VA research, even if the IRB determines it is exempt from the Common Rule.

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Exemption for Educational Research [38 CFR 16.101(b)(1)]

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

Exemption for Educational Tests, Surveys, Interviews, Observations [38 CFR 16.101(b)(2)]

- 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.

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Exemption for Research on Existing Data, Unlinked to Subjects [38 CFR 16.101(b)(4)]

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

Can Human Subjects Research be Reviewed by an *Expedited* process?

1. Must fit one or more of the expedited review categories, and be no more than minimal risk

-OR-

2. Minor changes in previously IRB approved research during the period for which the approval is authorized

VHA Handbook 1200.05, Paragraph 18

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What is *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 tests.

38 CFR 16.102(i)

HHS Secretary's Advisory Committee on Human Research Protections (SACHRP) : Understanding Minimal Risk (case examples)
www.hhs.gov/ohrp/sachrp/sachrpminrisk20080131.html

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Collected Materials (Expedited Review Category Number 5)

- Research involves:
  - Materials (data, documents, records, or specimens) that have been collected for any purpose, including previous research, or
  - Materials (data, documents, records, or specimens) that will be collected solely for nonresearch purposes (such as medical treatment or diagnosis.)

NOTE: Some research in this category may be exempt from the VA regulations for the protection of human subjects (38 CFR 16.101(b)(4)). This listing refers only to research that is not exempt.

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Collection of Data From Voice, Video, or Photographs for Research Purposes (Expedited Review Category Number 6)

- Collection of data from voice, video, or photographs for research purposes

Note: See paragraph 55 of VHA Handbook 1200.05 for additional information

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Group Characteristics, Surveys, Interviews, and Quality Assurance (Expedited Review Category Number 7)

- Research must be 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 will employ survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

NOTE: Some research in this category may be exempt from the VA regulations for the protection of human subjects (38 CFR 16.101(b)(2) and (b)(3)). This listing refers only to research that is not exempt.

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Activities Must Meet Expedited Review Criteria

- Cannot expedite when identification of the subjects or their responses would reasonably:
  - place them at risk of criminal or civil liability;
  - be damaging to the subjects' financial standing, employability, insurability, or reputation; or
  - be stigmatizing.
- Unless reasonable and appropriate protections are implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal.

VHA Handbook 1200.05, Paragraph 19

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Activities Must Meet Expedited Review Criteria

- IRB must apply the standard requirements for informed consent (or its waiver, alteration, or exception) to all studies that undergo expedited review.

VHA Handbook 1200.05, Paragraph 19

HHS Office of Human Research Protections (OHRP) Guidance*

- Human Subject Regulations Decision Charts;
- Guidance on Research Involving Coded Private Information or Biological Specimens;
- FAQs: Exempt Research Determination;
- Exempt Research and Research That May Undergo Expedited Review; and
- Categories of Research That May Be Reviewed by the IRB through an Expedited Review Procedure.

*www.hhs.gov/ohrp/policy/index.html

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VHA Office of Research & Development's (ORD) Program for Research Integrity Development & Education (PRIDE)

- Questions may be addressed to PRIDE:
  - Email: VHACO120005Q@va.gov
  - Website: www.research.va.gov/programs/pride

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Simulation Case Studies

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Simulation Case Study # 1

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Simulation Case Study # 1

- The Old Glory VA Medical Center conducts a simulation-based course to teach central line placement.
- For internal quality assurance, the facility Designated Learning Officer (DLO) wishes to determine if the course should be repeated in the same format.
- She surveys adult employee course participants to evaluate their satisfaction.
- She does not collect participant names.
- Her activities are not designed to expand scientific understanding or the knowledge base of a scholarly field.

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Simulation Case Study # 1: Q & A

- **Is the DLO conducting a systematic investigation?**
  - Yes:
    - activity planned in advance
    - activity uses data collection and analysis to answer a question
- **Is this activity designed to develop or contribute to generalizable knowledge?**
  - No:
    - activity is for internal operations only
    - will not expand the scientific understanding or the knowledge base of a scholarly field

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Simulation Case Study # 1: Q & A

- **Is this Research?**
  - No.
    - Knowledge is not generalizable.
- **Implications:**
  - Neither the IRB nor R&D Committee is required to review the activity.

Simulation Case Study # 2

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Simulation Case Study # 2

Same details as Case #1, plus:

- The DLO will pull “extra data” beyond participant satisfaction survey, such as patient outcomes for those who received the training.
- She will compare the course delivery process and patient outcomes to a similar course presented at The Red White & Blue VA.
- She plans to generalize the findings beyond VA and hopes to expand the knowledge base regarding the effectiveness of simulation for teaching central line placement.

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Simulation Case Study # 2: Q & A

- **Is this activity designed to develop or contribute to generalizable knowledge?**
  - Yes. The information will expand knowledge base of geriatrics.

- **Is this Research?**
  - Yes. Meets criteria for “systematic investigation” and “generalizable knowledge”.

Simulation Case Study # 2: Q & A

- **Does the research involve obtaining information about living individuals?**
  - Yes. Information pertains to living individuals because the DLO is collecting participants' opinions and extra data such as patient outcomes (which may be individually identifiable.)
- **Does the research involve an intervention or interaction with the individuals?**
  - Yes. Surveys represent an interaction.
- **Is the information individually identifiable?**
  - No. The participant names are not on the survey.

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Simulation Case Study #2: Q & A

- **Is the activity research involving human subjects?**
  - Yes, because the investigator obtains information through an interaction.

Simulation Case Study # 2: Q & A

- **Is this activity eligible for exemption(s)?**
  - It depends – more information is needed for the IRB to make the determination.

Simulation Case Study # 2: Q & A

- **Exemption categories that might apply :**
  - Exempt category #1 may apply if research is conducted in established/commonly accepted educational settings, involving normal educational practices.
  - Exempt category #1 may **not** apply to the accessing of patient outcomes.

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Simulation Case Study # 2: Q & A

- **Exemption categories that might apply :**
  - Exempt category #2 may apply if research involves surveys with *adults* when the information collected about the participants is "sensitive/risky*" or "identifiable" (but not *both* "sensitive/risky" and "identifiable".)
  - Exempt category #2 may **not** apply to the accessing of patient outcomes.

*(e.g., could employees' jobs be jeopardized if their responses to the survey become public?)

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Simulation Case Study # 2: Q & A

- **Is this activity eligible for expedited review?**
  - It depends – more information is needed for the IRB to make the determination.
    - Expedited review category #7 may apply if the IRB determines:
      - Activities meet expedited review criteria*, and
      - Research involves individual/group characteristics/behavior, surveys, interviews, quality assurance, etc.

*(e.g., could employees' jobs be jeopardized if their responses to the survey become public?)

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Simulation Case Study # 2: Q & A

- **Implications:**
  - **Exempt:** The IRB, not the investigator, needs to make the exempt determination.
  - **Expedited:** If the project is not exempt, the IRB may choose to use the expedited review process if the project is eligible for expedited review.
  - **Convened:** If human subjects research is not eligible for exemption or expedited review, it must be reviewed by convened IRB.

Simulation Case Study # 3

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Simulation Case Study # 3

- Dr. Three wants to conduct research on how long it takes a nurse to act in a respiratory depression patient-care situation.
- She requests copies of video recordings that were taken of nurses during respiratory depression simulations that were intended to be used for debriefing with the learners.
- The simulationist agrees to provide the videos with faces blurred out to protect the participants.
- Unfortunately, Dr. Three can readily ascertain the identity of the learners.

Simulation Case Study # 3: Q & A

- **Is this Research?**
  - It depends on whether the information will expand a knowledge base outside the VA.
    - If no, this is not research.
    - If yes, it is research.
  - Let us assume this project meets criteria for “systematic investigation” and “generalizable knowledge” (i.e., that it is research.)

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Simulation Case #3: Q & A

- **Does the research involve obtaining information about living individuals?**
  - Yes. Information pertains to living individuals (i.e., the nurses.)
- **Does the research involve an intervention or interaction with the individuals?**
  - No. The investigator does not intervene or interact with individuals in the video (videos already existed.)
- **Is the information individually identifiable?**
  - Yes. Dr. Three can readily ascertain the identity of individuals in the video.

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Simulation Case Study # 3: Q & A

- **Is the information private?**
  - Yes.
    - Learners can reasonably expect that their learning video will not be made public.
    - The recordings do not take place in a public setting.
- **Is the activity research involving human subjects?**
  - Yes. Dr. Three is obtaining individually identifiable private information about living individuals (i.e., Dr. Three can recognize the nurses even though the faces have been blurred.)

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Simulation Case Study # 3: Q & A

- **Is this activity eligible for exemption(s)?**
  - It depends – more information is needed for the IRB to make the determination.
    - Exempt category #1 may apply if research is conducted in established/commonly accepted educational settings, involving normal educational practices.

Note: For exempt Category #1 to apply, Dr. Three's project must have an educational purpose.

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Simulation Case Study # 3: Q & A

- **Is this activity eligible for expedited review?**
  - It depends – more information is needed for the IRB to make the determination.
    - Expedited review category #5 may apply if the IRB determines:
      - Activities meet expedited review criteria, and
      - Research involves only materials that were collected for other purposes or for previous research.
  - Expedited review category #6 does not apply because these videos were not created for research purposes.

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Simulation Case Study #3: Q & A

- Expedited review category #7 may apply if the IRB determines:
  - Activities meet expedited review criteria, and
  - Research involves individual/group characteristics or behavior or will employ survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Note: If Dr. Three is just measuring reaction times, not individual/group characteristics, then category #7 would not apply.

Simulation Case Study # 3: Q & A

- **Implications:**
  - **Exempt:** The IRB, not the investigator, needs to make the exempt determination.
  - **Expedited:** If the project is not exempt, the IRB may choose to use the expedited review process if the project is eligible for expedited review.
  - **Convened:** If human subjects research is not eligible for exemption or expedited review, it must be reviewed by convened IRB.

Simulation Case Study # 4

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Simulation Case Study # 4

- Dr. Four wants to conduct research in the simulation lab on a debriefing study.
- He will use previous video recordings done in the simulation lab from an old Advanced Cardiac Life Support (ACLS) case and debriefing session.
- The ACLS case was a code scenario from the Emergency Department (ED) setting in which a 72 year old woman was brought to the ED unresponsive and in cardiac arrest.
- The monitor strip showed asystole, and the team worked on the resuscitation.

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Simulation Case Study #4

- A 15 minute debriefing session followed the case for all learners involved.
- All of the materials are existing at the time of the proposal and have been previously recorded.
- Dr. Four could recognize the learners in the video but not the 72 year old woman; however, he will record data (debriefing items) in a spreadsheet in such a manner that subjects cannot be identified.

Simulation Case Study #4

- All the data will be used only by his research team.
- Following the study, the recordings will be deleted or entered back into the archive.
- No one will be able identify the 72 year old woman or learners by looking at the spreadsheet, including Dr. Four.

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Simulation Case Study # 4: Q & A

- **Is this Research?**
  - It depends on whether the information will expand a knowledge base outside the VA.
    - If no, this is not research.
    - If yes, it is research.
  - Let us assume this project meets criteria for “systematic investigation” and “generalizable knowledge” (i.e., that it is research.)

Simulation Case Study #4: Q & A

- **Does the research involve obtaining information about living individuals?**
  - Yes. Information pertains to living individuals (i.e., the learners.)
- **Does the research involve an intervention or interaction with the individuals?**
  - No. Dr. Four does not intervene or interact with the learners or the patient in the video.

Simulation Case Study # 4: Q & A

- **Is the information individually identifiable?**
  - Yes, because Dr. Four was able to identify the learners while he was making his spreadsheet.
- **Is the information private?**
  - Yes. The learners can reasonably expect that information will not be made public.

Simulation Case Study # 4: Q & A

- **Is this activity research involving human subjects?**
  - Yes. Dr. Four is obtaining individually identifiable private information about living individuals (i.e., even though he may return the videos after recording the information, the private information can be associated with the individuals because their faces are not blurred out in the video.)

Simulation Case Study #4: Q & A

- **Is this activity eligible for exemption(s)?**
  - It depends – more information is needed for the IRB to make the determination.
    - Exemption category #4 may apply if Dr. Four records the information in a de-identified manner and does not create any key that allows identification of the subjects.

Simulation Case Study #4: Q & A

- **Is this activity eligible for expedited review?**
  - It depends – more information is needed for the IRB to make the determination.
    - Expedited review category #5 may apply if the IRB determines:
      - Activities meet expedited review criteria, and
      - Research involves only materials that were collected for other purposes or for previous research.

Simulation Case Study # 4: Q & A

- **Implications:**
  - **Exempt:** The IRB, not the investigator, needs to make the exempt determination.
  - **Expedited:** If the project is not exempt, the IRB may choose to use the expedited review process if the project is eligible for expedited review.
  - **Convened:** If human subjects research is not eligible for exemption or expedited review, it must be reviewed by convened IRB.

Simulation Case Study # 5

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Simulation Case Study #5

- Dr. Five wants to compare communication styles of physician-nurse teams caring for a critically-ill patient.
- A mannequin-based scenario is designed in which a 72 year-old patient (mannequin) is showing early signs of sepsis secondary to a perforated colon.
- The patient is in pain and the family member (confederate) is distraught.
- In managing the patient, the providers must also communicate effectively with each other and with the family member.
- The scenario is recorded to debrief participants regarding the care of the patient.

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Simulation Case Study #5

- The recordings are reviewed to document characteristics of communication style.
- Each provider who participates in the simulation signs a consent form giving permission for the recording of the event and analysis of the communication styles for research.
- The consent includes the disposition of the recordings and assurance that the analyses are confidential and will not be used for any professional or personnel actions.

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Simulation Case Study #5: Q & A

- **Is this research?**
  - It depends on whether the information will expand a knowledge base outside the VA.
    - If no, it is not research.
    - If yes, it is research.
- Let us assume it meets criteria for “systematic investigation” and “generalizable knowledge” (i.e., that this project is research.)

Simulation Case Study # 5: Q & A

- **Does the research involve obtaining information about living individuals?**
  - Yes. Information pertains to living individuals (i.e., the learners.)
- **Does the research involve an intervention or interaction with the individuals?**
  - Yes. Videotaping the providers is an interaction.
- **Is the information individually identifiable?**
  - Yes, to Dr. Five.

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Simulation Case Study #5: Q & A

- **Is the information private?**
  - Yes.
    - The providers can reasonably expect that their learning video will not be made public.
    - The recordings do not take place in a public setting.
- **Is the activity research involving human subjects?**
  - Yes. Dr. Five is obtaining individually identifiable private information about the providers.

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Simulation Case Study # 5: Q & A

- **Is this activity eligible for exemption(s)?**
  - It depends – more information is needed for the IRB to make the determination.
  - Exemption category #1 may apply if the IRB determines the research conducted in established/commonly accepted educational settings, involving normal educational practices.

Simulation Case Study # 5: Q & A

- **Is this activity eligible for expedited review?**
  - It depends – more information is needed for the IRB to make the determination.
    - Expedited review category #6 may apply if the IRB determines:
      - Activities meet expedited review criteria, and
      - Research involves only the collection and analysis of images or voice recordings.

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Simulation Case Study #5: Q & A

- Expedited review category #7 may apply if the IRB determines:
  - Activities meet expedited review criteria, and
  - Research involves individual/group characteristics or behavior or will employ survey, interview, oral history, focus group, program evaluation, human factors evaluation, or quality assurance methodologies.

Simulation Case Study # 5: Q & A

- **Implications:**
  - **Exempt:** The IRB, not the investigator, needs to make the exempt determination.
  - **Expedited:** If the project is not exempt, the IRB may choose to use the expedited review process if the project is eligible for expedited review.
  - **Convened:** If human subjects research is not eligible for exemption or expedited review, it must be reviewed by convened IRB.

Summary
The Key Questions to Ask in the Following Order

Answer questions in proper sequence when determining whether an activity is research, human subjects research, exempt, or can be expedited.

1. Is this project **research**?
2. If so, does it involve **human subjects**?
3. If so, is it **exempt**?
4. If it is not exempt, is it eligible for ***expedited*** review?

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THE DEVIL IS ALWAYS IN THE DETAILS

- Overlooking or changing one detail of the protocol could change the determination from:
  - research to human subjects research.
  - exempt to requiring expedited IRB review.
  - expedited IRB review to requiring convened IRB review.
- All details of the project must be taken into consideration before these determinations can be made.

QUESTIONS

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