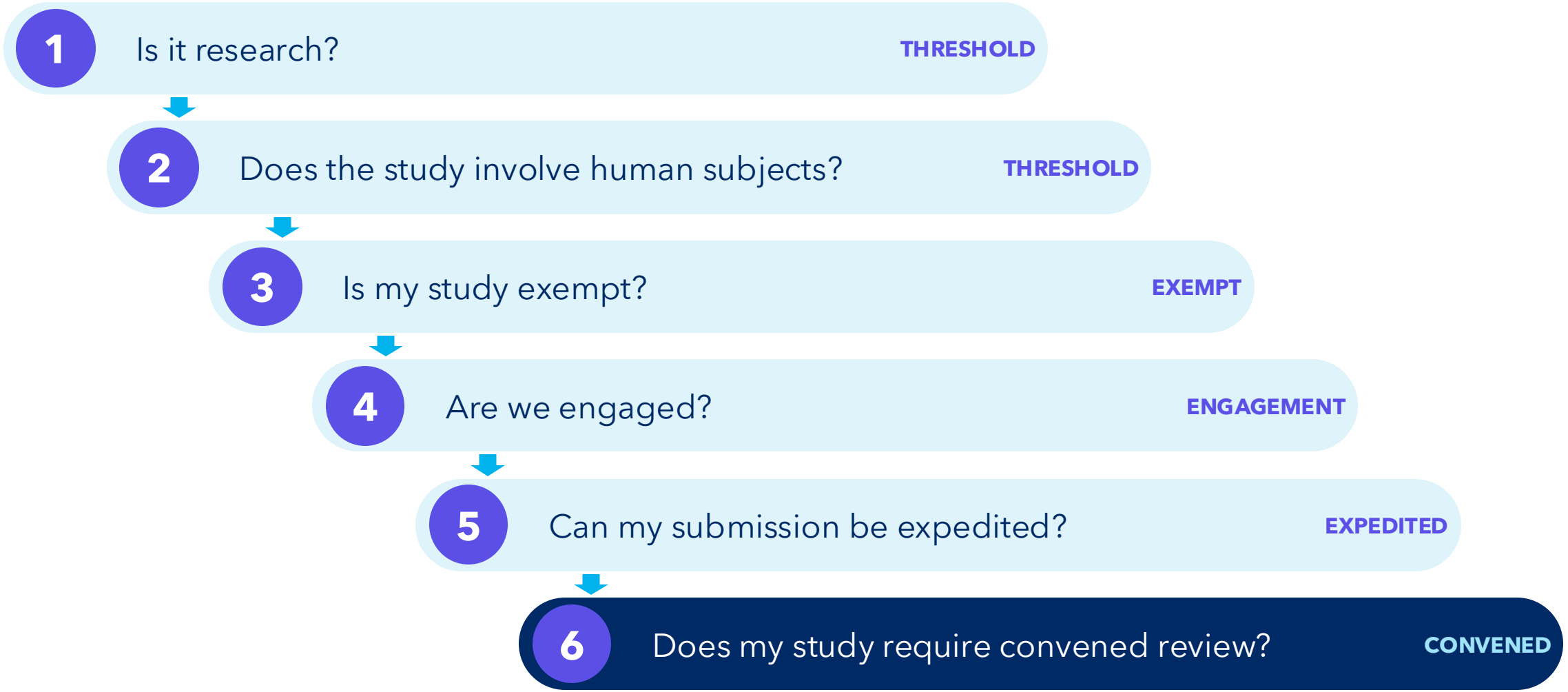
A WEBINAR SERIES

IRB 101: Levels of Review



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Your Roadmap: Six Questions to the Right Level of Review



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Meet Your Speakers



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1. Is it research?

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Is It Research?

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



Systematic investigation

Likely involves a hypothesis or research question, and a plan to systematically collect and analyze data.

45 CFR 46.102



Generalizable knowledge

The systematic investigation adds information and contributes to generalizable knowledge in the field.

Whether or how an investigator shares results with the scientific community is not the deciding factor for whether the activity was designed to develop or contribute to generalizable knowledge.

45 CFR 46.102

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Is It Research?

Research: a systematic investigation

- Prospective or Retrospective
- Hypothesis
- Plan (Protocol)
- Single Patient Case Reports
- Editorial Comments/SME Recommendations

Generalizable Knowledge

Study collecting information about customer's satisfaction or experiences with a product.

- *Obj. 1*: guide purchasing decisions
- Obj. 2: determine usability/performance of the product

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Is It Research?

Not Research

- Scholarly and journalistic activities that focus on information specifically about certain individuals
- Certain public health surveillance activities
- Certain activities solely for criminal justice or criminal investigative purposes
- Certain operational activities in support of national security missions

45 CFR 46.102 (l)

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2. Does the study involve human subjects?

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Is it Research Involving Human Subjects?

A **living** individual about whom an investigator (whether professional or student) is conducting research:

(i) Obtains information or biospecimens through **intervention or interaction** with the individual, and, uses studies, or analyzes the information or biospecimens; or
(ii) Obtains, uses, studies, analyzes, or generates **identifiable** private information or identifiable biospecimens.

Intervention	*Drawing blood, measuring blood pressure, request to follow specific diet, changing light in the room*
Interaction	*Interviews, surveys, focus groups*
Private Information	*Medical records, school records, personal financial information*
Identifiable PI and specimens	*Names, SSN, address, email, codes that links to identifiers*

45 CFR 46.102

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Is it Research Involving Human Subjects?

RESEARCH + **HUMAN SUBJECT** → **REVIEW PATHS**

1 Scenario 1

A researcher plans to review medical records from 100 **deceased** patients to study the effects of the treatment on their tumor progression.

2 Scenario 2

The local jail is implementing a Systems Analysis and Improvement Approach (SAIA) project to try to improve linkage to Medications for Opioid Use Disorder (MOUD) care post release. The project will start before prisoners are released and will follow them for three years after release to evaluate the percentage of prisoners who successfully are linked to MOUD care. Training the health care workers on SAIA intervention, and implementing the intervention are part of a Quality Improvement Initiative by the local jail.

3 Scenario 3

A researcher plans to review retrospective information and collect leftover samples of mothers and their babies, and will use identifiable information to contact mothers to complete questionnaires.

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3. Is my study exempt?

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Is the Research Exempt from IRB Review?

(a)

Exempt research must still meet this section's requirements and each category's conditions, unless law or agency heads say otherwise.

(d)

The (d) categories of human subjects research are exempt from the policy. The next slides walk through them.

45 CFR 46.104

"Exempt" means exempt from the Common Rule's requirements, **not from a determination.**

Someone other than the investigator decides, usually the IRB office.

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Exemption (d)(1): Educational Settings

45 CFR 46.104(d)(1)

- Established or commonly accepted educational settings
- Involves normal educational practices
- Not likely to adversely impact students' opportunity to learn required content or the assessment of educators

Is this something the school would **do anyway?**

If the study doesn't change what students are taught or how educators are assessed, it may qualify.

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Exemption (d)(2): Surveys, Interviews, Observation

45 CFR 46.104(d)(2)

Research that only involves educational tests, surveys, interviews, or observation of public behavior, and meets at least one criterion:

(i) Identity cannot readily be ascertained.

(ii) Disclosure would not risk liability or damage finances, employability, education, or reputation.

(iii) Identifiable, with limited IRB review under §46.111(a)(7).

Identifiable data isn't **automatically ruled out.**

Criterion (iii) covers identifiable data, with limited IRB review. For children, interviews and surveys don't qualify.

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Exemption (d)(3): Benign Behavioral Interventions

45 CFR 46.104(d)(3)(i)

Benign behavioral interventions with data collection from an **adult** subject, if the subject prospectively agrees and at least one criterion is met:

a) Identity cannot readily be ascertained.

b) Disclosure would not risk liability or damage subjects' standing or reputation.

c) Identifiable, with limited IRB review under §46.111(a)(7).

Adults only, and **agreement comes first.**

Children can't be enrolled under (d)(3), and subjects must agree before the intervention, not after.

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Exemption (d)(3) Continued: Benign and Deception

45 CFR 46.104(d)(3)(ii-iii)

(ii) Benign: brief, harmless, painless, not physically invasive, no significant lasting adverse impact, and not offensive or embarrassing.

Examples: An online game, puzzles solved under different noise conditions, or asking the subject to allocate a nominal amount of cash.

(iii) Deception: the exemption does not apply unless subjects authorize it through a prospective agreement to be unaware of or misled about the research.

Benign means all of it, **not most of it.**

Doubt any one criterion and the intervention isn't benign. Document your rationale for each one.

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Exemption (d)(4)

45 CFR 46.104(d)(4)

(4) Secondary research for which consent is not required: Secondary research uses of identifiable private information or identifiable biospecimens, if at least one of the following criteria is met:

i. The identifiable private information or identifiable biospecimens are publicly available.

ii. Information, which may include information about biospecimens, is 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.

iii. The research involves 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 the purposes of "health care operations" or "research" as those terms are defined at 45 CFR 164.501 or for "public health activities and purposes" as described under 45 CFR 164.512(b) or.

iv. The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for non-research activities, if the research generates identifiable private information that is or will be maintained on information technology that is subject to and in compliance with section 208(b) of the E-Government Act of 2002, 44 U.S.C. 3501 note, if 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, 5 U.S.C. 552a, and, if applicable, the information used in the research was collected subject to the Paperwork Reduction Act of 1995, 44 U.S.C. 3501 et seq.

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Exemption (d)(4): Secondary Research

45 CFR 46.104(d)(4)

Secondary research uses of identifiable private information or biospecimens, if at least one criterion is met:

i. Publicly available.

ii. Identity cannot readily be ascertained; no contact; no re-identification.

iii. Identifiable health information regulated under HIPAA (45 CFR 160 and 164) for health care operations, research, or public health.

iv. Federal agency research using government-collected information, with privacy-law safeguards.

What you can access decides it, **not the label.**

A dataset called “de-identified” can still fall outside this category if you hold a key or can link it back to individuals.

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Additional Exempt Categories

EXEMPT

5

Federal research or demonstration project designed to examine public benefit or service programs.

EXEMPT

6

Taste and food quality.

EXEMPT

7&8

Broad consent.

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4. Are we engaged?

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Are we engaged?

Engagement of Institutions in Human Subjects Research (HHS)

An institution is engaged when its employees or agents, for the purposes of the research, obtain:

1. Data about subjects through intervention or interaction with them.

2. Identifiable private information about subjects.

3. Informed consent from subjects for the research.

Engagement is about what a site's staff do, **not whether it is listed.**

Sites that are not engaged in research don't require IRB review. OHRP guidance describes which institutions are and aren't engaged.

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Not Engaged: Commercial or Other Services

Engagement of Institutions in Human Subjects Research (HHS)

Not engaged if involvement is limited to services performed for investigators, and all of these are met:

a) The services do not merit professional recognition or publication privileges.

b) They are typically performed by the institution for non-research purposes.

c) Its employees or agents do not administer any study intervention.

Being the study setting **isn't the same as being engaged.**

A hospital where researchers observe and interview, but whose own staff are not involved in the study or collecting data, is not engaged.

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Not Engaged: Recruitment Support

Engagement of Institutions in Human Subjects Research (HHS)

Not engaged if employees or agents only do the following, without obtaining consent or acting for the investigators:

a) Inform prospective subjects about the research.

b) Provide information, which may include the IRB-approved consent form.

c) Provide contact information for investigators.

d) Seek permission for investigators to contact them.

Handing out the consent form **isn't obtaining consent.**

A recruitment firm can share study information and the consent form. When participants sign at their on-site visit, the firm is not a research site.

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Not Engaged: One-Time or Short-Term Care

Engagement of Institutions in Human Subjects Research (HHS)

Not engaged if an institution not selected as a research site administers study interventions on a one-time or short-term basis, and all of these are met:

a) An engaged investigator decides it is in the subject's best interest.

b) Its staff do not enroll subjects or obtain consent.

c) Engaged investigators keep responsibility for oversight, protocol-compliant administration, and data and safety reporting.

d) An IRB on the engaged institution's FWA is informed.

A one-time stop elsewhere **doesn't make that facility a research site.**

If a participant is traveling and gets a standard-of-care infusion at another facility, the study team stays responsible and the IRB is told.

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5. Can my submission be expedited?

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Expedited Review

OHRP Expedited Review: Categories of Research (1998)

To qualify for expedited review, the study must meet both requirements:

1. Minimal risk

2. On the list of activities eligible for expedited review

Minimal risk alone **is not enough.**

A minimal risk study still needs convened full board review if its activities are not on the eligible list.

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Expedited Review: Key Definitions

Expedited review **is not an expedient review.**

It may not be a quicker turnaround time than full board review.

Expedited review

Conducted by one or more designated IRB members. Applies to minimal-risk research.

Full board review

Requires convened review by the entire IRB committee. Required for studies involving greater-than-minimal risk, including most clinical trials.

Minimal risk 45 CFR 46.102(i); 21 CFR 50.3(k)

"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."

The risks are those, that a healthy person could expect to encounter at routine clinical visits.

Minimal risk does not mean that the risks of a drug, device or procedure is minor or acceptable given the condition being treated.
Minimal risk does not equate to risk assessment in clinical care.

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Expedited Review: Other Considerations

Other considerations *(besides minimal risk and on the list)*

Expedited Review: Categories of Research (1998)

Regardless of age

The categories apply regardless of age, except as specified in the list.

Excludes classified research

Classified research is not eligible for expedited review.

Expedited review may not be used where:

Identification of the subjects and/or their responses would reasonably place them at risk of criminal or civil liability, or be damaging to their financial standing, employability, insurability or reputation, or be stigmatizing.

Unless reasonable and appropriate protections will be implemented so that risks related to invasion of privacy and breach of confidentiality are no greater than minimal risk.

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Expedited Category 1: Drugs and Devices

1. Clinical studies of drugs and/or medical devices only when:

a) An IND (investigational new drug application) is not required.

b) An IDE (investigational device exemption application) is not required.

c) The medical device is cleared/approved for marketing and is being used in accordance with the cleared/approved indications.

Exception

Any research involving legally marketed drugs that significantly increases the risks or decreases the acceptability of the risks associated with the use of the product is not eligible for expedited review and will require review by a convened board.

Drug Example: *When an FDA-approved drug is being administered as a research procedure, this usually requires full board review.*

Device example: *An in vitro diagnostic device when test results are not being returned to participants or clinicians, if the result does not affect management, diagnosis, or treatment decisions may be expedited.*

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Expedited Category 2: Blood Draws

2. Collection of blood samples by finger stick, heel stick, ear stick, or venipuncture from:

Healthy, nonpregnant adults who weigh at least 110 pounds. The amounts drawn cannot be more than 550 ml in an eight-week period, and no more than two blood collections are allowed per week.

Other adults and children. The amounts drawn must be less than 50 ml or 3 ml per kg (whichever is lesser) per eight-week period, and no more than two blood collections are allowed per week.

IRB needs to know:

If blood samples are being taken, the protocol should include:

Who: population group (age, pregnant participants, healthy and diseased participants).

How: drawn from an existing line versus insertion of a line.

What: venous or arterial blood.

Quantity: amount of blood in volume.

Frequency: how often; if more than once, how many days apart.

This will prevent delays in review time.

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Expedited Category 3: Biological Specimens

3. Prospective collection of biological specimens intended for research purposes if:

The collection is noninvasive.

Examples:

- Urine specimens, saliva samples, fingernail or hair clippings
- Placenta after delivery
- Sputum collected after saline mist nebulization

Only anterior nasal swabs **are noninvasive.**

Any mid turbinate nasal swab requires full board review, as it is considered invasive by FDA.

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Expedited Category 4: Data Collection

4. Collection of data if:

a) The procedure collecting the data is noninvasive and cannot require sedation or anesthesia as research procedures.

b) The procedure is routinely employed in clinical practice and cannot involve X-rays, microwaves, or require the use of contrast.

c) If a medical device is being used, it 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. This includes studies of cleared medical devices for new indications.)*

Examples of data collection

(a) Physical sensors applied to the surface of the body or at a distance that do NOT involve input of significant amounts of energy into the subject or an invasion of the subject's privacy

(b) Weighing or testing sensory acuity

(c) Magnetic resonance imaging

(d) Electrocardiography, electroencephalography, thermography, detection of naturally occurring radioactivity, electroretinography, ultrasound, diagnostic infrared imaging, Doppler blood flow, and echocardiography

(e) Moderate exercise, muscular strength testing, body composition assessment, and flexibility testing where appropriate given the age, weight, and health of the individual

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Expedited Category 5: Existing Materials

5. Research involving materials that have been collected:

a) Retrospectively for any purpose. Examples: data, documents, records, or specimens.

OR

b) Prospectively, solely for non-research purposes. Examples: medical treatment or diagnosis.

For prospective collection

This needs to be the use of data that is collected about medical treatment that is occurring regardless of the research.

The procedure, treatment and/or the use of the drug or device cannot be dictated by the protocol.

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Expedited Categories 6 and 7

6. Collection of data from:

- Voice recordings
- Video recordings
- Digital or image recordings made for research purposes

7. 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.

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Expedited Review: Minimal Risk Examples

Examples of procedures that are generally considered to meet the minimal risk threshold include:

- Blood sampling from a vein or indwelling line (provided the volume and frequency of blood draw meets the criteria previously described)
- MRI without contrast and without sedation
- “Surface” (external only) imaging, without the use of contrast agents
- Placement of a peripheral venous line for less than 24 hours

Examples of Minimal risk procedures, that are not on the list of expeditable activities:

- Massage
- Meditation
- Listening to calming music
- Simulators: Driving car or flying plane
- Riding bicycles on different routes

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Expedited Review: Not Minimal Risk

Examples of procedures that are *not* considered to be minimal risk include:

- Administration of virtually any investigative drug or biologic as a research procedure, even if the product is approved for the indication being studied or for other indications and is known to have a generally mild safety profile and adverse events are rare.
- A clinical investigation of a device that involves invasive sampling

Procedures and imaging:

- MRI with contrast and/or sedation
- PET scans, or Transcranial Magnetic Stimulation (TMS) or other direct brain stimulation techniques.
- PICC / central line / arterial line
- CT scan
- Dexa scan to measure bone mineral density & body composition)

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6. Does my study require convened review?

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Full Board Review

Full board review by a convened Institutional Review Board (IRB) is **required for human subjects research that exceeds "minimal risk" or does not qualify for exempt or expedited review.**

This determination is usually the clearest to establish.

Everything that doesn't meet the previous criteria:

- More than minimal risk research based on the use of an investigational drug, device or research procedure.
- Non-Significant Risk device
- Research that is not on the list previously described.
- Previously disapproved or deferred research
- Invasive sampling (bone marrow biopsy, spinal tap, muscle biopsy, skin biopsy requiring suturing)

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Putting It Into Practice

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Before choosing a review pathway, document these seven things

7

things to document before you choose a review pathway

Capture the facts first so the right level of review follows.

Purpose	What is the activity intended to accomplish?
People	Who is involved, and in what capacity?
Interaction	What will researchers do with or to participants?
Information	What information or biospecimens will be obtained?
Identifiability	Who can connect the data to an individual, and when?
Risk	What could happen if the information were disclosed or the intervention went poorly?
Institutional role	Which organizations or individuals are performing which activities?

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The cost of getting the review pathway wrong



REWORK

Rework when project documents describe the activity inconsistently



DELAYS

Delays caused by missing information or an incorrect initial pathway



CONFUSION

Confusion over which institutions or partners require review



WEAK RECORDS

Difficulty relying on a determination that was not formally documented



LATE CHANGES

Changes to recruitment, consent, data access, or operational roles late in planning



COMPLIANCE RISK

Compliance risk when research activities begin before the appropriate determination or review

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Six principles for navigating IRB levels of review



ACTIVITY

Start with the activity, not the label.



SEQUENCE

Separate the regulatory questions and answer them in order.



RISK AND ROLES

Pay attention to identifiability, disclosure risk, and institutional roles.



LOCAL PROCESS

Expect local process differences even when the federal definitions are the same.



DOCUMENTATION

When facts are ambiguous, document the determination rather than relying on assumption.



TEAM REVIEW

Consult with the full team to ensure accuracy and completeness of the submission.

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AUDIENCE POLL

Would you like to connect with WCG about your IRB needs?

YES

NO

Select YES in the poll panel and our team will reach out to you.

Audience Q&A

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Thank you!

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