

# The ABCs of 104: Understanding Exemption Categories

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HHS Office for Human Research Protections ([OHRP](#))  
Division of Education and Development ([DED](#))



**OASH**

Office for  
Human Research  
Protections



# Disclaimer

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The opinions expressed are those of the presenter and do not necessarily reflect the policy of the U.S. Department of Health and Human Services.

For a complete and accurate description of the regulatory requirements, please refer to the text of the [revised Common Rule](#) available on OHRP's website.



# Learning Objectives

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- Discuss what ***exemption*** means
- Describe the exemptions in the Common Rule
- Explain the conditions needed to qualify for the more commonly used exemption categories



# When Do Regulatory Requirements Apply and What Does That Mean?

## Regulatory Requirements Apply

When a project is  
***Nonexempt Human Subjects Research***

This means (among others):

- IRB review according to regulatory requirements & criteria
- Informed consent according to regulatory requirements (unless waived)

## Requirements Typically Do NOT Apply

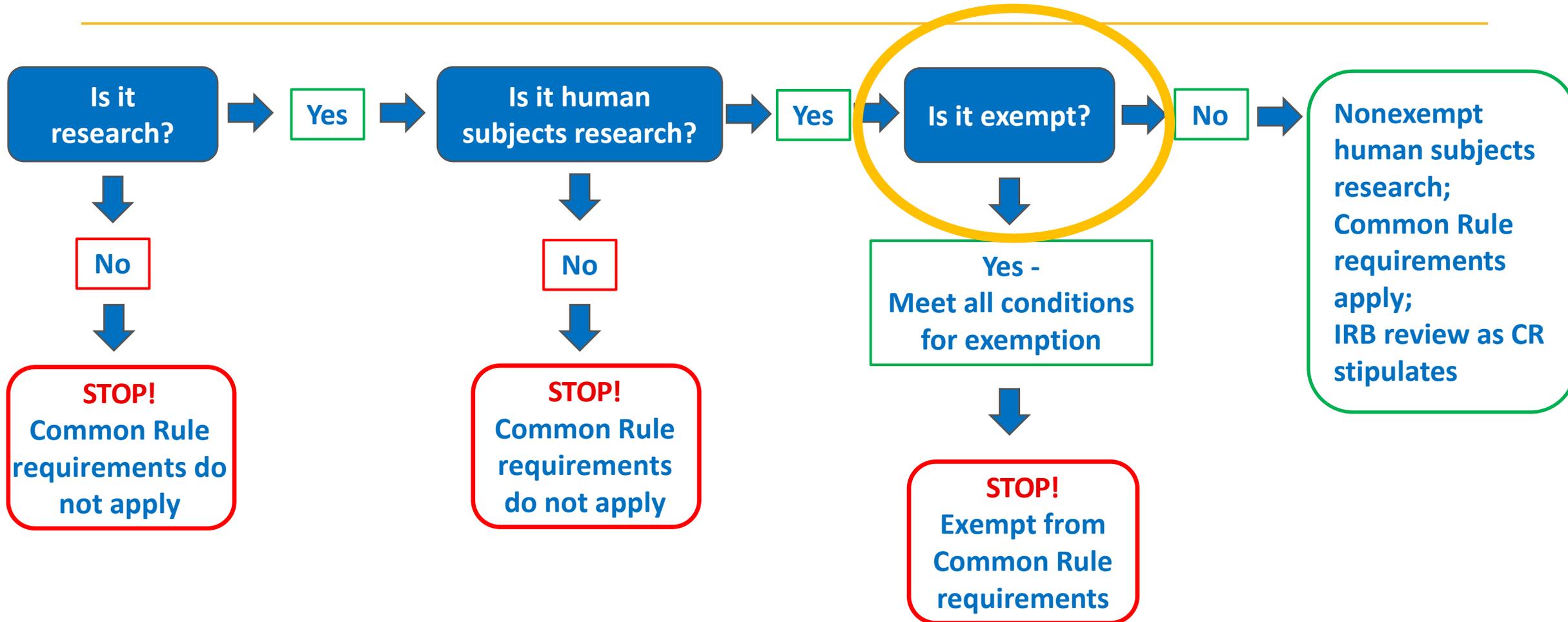
- When a project is ***not Research***, or
- When a project is ***not Human Subjects Research***, or
- When a project is ***Exempt Human Subjects Research***



Investigators/Institutions have  
**Flexibility** outside the regulations



# Flowchart Showing How to Determine if a Project is *Nonexempt Human Subjects Research*



# What Does It Mean That Research Is “Exempt”?

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- The study meets the regulatory definition for **human subjects research** but satisfies the conditions for one or more of the eight exempt categories described in the Common Rule
- Exempt studies are excused from the typical requirements of the Common Rule, such as, IRB review according to the criteria at 46.111 and the informed consent requirements at 46.116
  - There may be a special limited IRB review
- Institutions generally rely on experienced individuals in the IRB office to make exemption determinations instead of leaving this to investigators
  - Making exemption determinations ≠ IRB review and approval



# Quick Overview of the Eight *Exempt Categories*

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Exemption 1: Normal educational practices in established educational settings

Exemption 2: Educational tests, surveys, interviews, or observation of public behavior

Exemption 3: Benign behavioral interventions

Exemption 4: Secondary research use of biospecimens or information for which informed consent is not required

Exemption 5: Evaluation of public benefit and service programs

Exemption 6: Taste and food quality evaluation & customer acceptance studies

Exemption 7: Storage and maintenance of identifiable materials for unspecified secondary research with broad consent

Exemption 8: Secondary research use of stored identifiable materials with broad consent

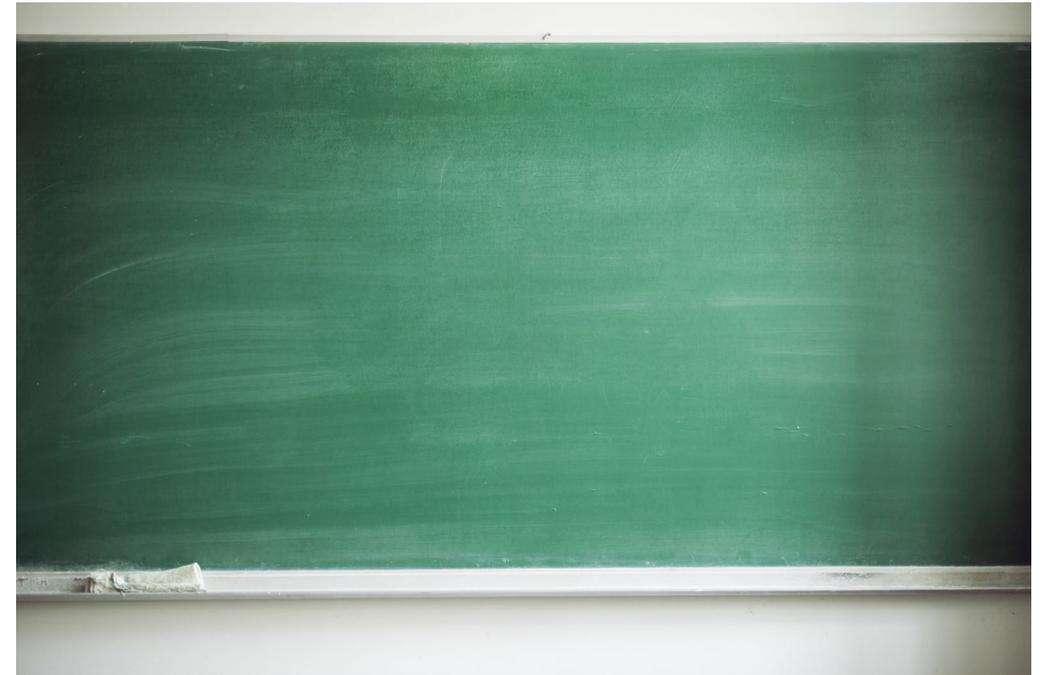
\*none are applicable to prisoners, \*\*some exemptions many not apply to children



## Exemption 1 at §46.104(d)(1)

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- Research, conducted in established or commonly accepted **educational settings**, that
- involves **normal educational practices**
- that are **not likely** to adversely impact students' opportunity to learn required educational content or
- the assessment of educators who provide instruction.



## Exemption 1: Example 1

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A researcher believes frequent breaks from instruction leads to better retention of historical facts. The researcher has a teacher use five out of every twenty minutes of a history class to let the students draw and compares test results to a second class where the students only receive history instruction.

- Educational setting? ✓ (Yes)
- Normal educational practice? ✓ (Yes)
- Not adversely impact learning required content? ✗ (No)

➤ **No, exemption 1 probably does not apply**



## Exemption 1: Example 2

A researcher wants to know if medical students can learn just as effectively from actors mimicking symptoms as they can from real patients. She follows and observes a group of students from a medical school that currently uses actors in exam rooms and a second group from a medical school that only uses real patients in its teaching hospital. She rates students' interactions and compares students' scores on a licensure exam.

- Educational setting? ✓ (Yes)
- Normal educational practice? ✓ (Yes)
- Not adversely impact learning required content? ✓ (Yes)

➤ **Yes, exemption 1 probably does apply**



## Exemption 2 at §46.104(d)(2)

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Research that only includes interactions involving educational tests (cognitive, diagnostic, aptitude, achievement), **survey procedures\***, **interview procedures\***, or observation of public behavior

- i. the identity of the human subjects cannot readily be ascertained, OR
- ii. 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 OR
- iii. the identity of the human subjects can readily be ascertained AND an IRB conducts a limited IRB review\*

(\*These may **NOT** be used with research involving children!)



# What is Limited IRB Review?

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- This is **not** the standard IRB review required by the CR for nonexempt human subjects research; no need to review according to the review criteria at 46.111
- Reviewer is ONLY asked to ensure that the conditions stipulated for the exemption are fully met
- Specifically for exemptions 2(iii) and 3(C), this is:
  - *When appropriate, there are adequate provisions to protect the **privacy of subjects** AND to maintain the **confidentiality of data**. (as referenced at 46.111(a)(7), emphasis added).*
- Review is done by a designated member of the IRB
- It is usually a one-time review with no requirement for regular continuing reviews
- However, any change to the protocol would likely require a re-review to determine that the conditions for the exemption are still met



## Exemption 2: Examples 1 & 2

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A researcher wants to interview adult residents at a drug rehabilitation center to learn about their prescription drug addiction. The researcher will record the responses without any personal data and then publish findings in aggregate.

- Is this activity an interaction covered by Exemption 2? ✓ (Yes)
  - Do the data include readily identifiable subjects' information? ✗ (No)
- **Yes, exemption 2 would likely work**

The researcher decides to expand the original study to include juveniles.

- Is this type of interaction allowed with children in exemption 2? ✗ (No)
- **No, exemption 2 would not apply**



## Exemption 2: Example 3

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A researcher wants to interview adult residents at a drug rehabilitation center to learn about their prescription drug addiction. Participants will wear a heart monitor to see if any questions elicit an elevated heartbeat. The researcher will record the responses without any personal data and then publish findings in aggregate.

- Are all activities interactions covered by Exemption 2? **X** (No)
- **This study now involves also an intervention. Exemption 2 does not apply.**



## Exemption 3 at §46.104(d)(3)

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Research involving **benign behavioral interventions** and **data collection** through verbal or written responses including audiovisual recordings if the adults agree prospectively, if one of the three applies:

- A. the identity of the human subjects cannot readily be ascertained, OR
- B. disclosure of the human subjects' responses outside the research would not reasonably place the subjects at risk OR
- C. the identity of the human subjects can readily be ascertained AND an IRB conducts a limited IRB review

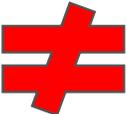
\*\*\* Exemption 3 is **NOT** to be used when the research is with **CHILDREN**\*\*\*



## Exemption 3 (CONT.)

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Research involving **benign behavioral interventions** and **data collection** through verbal or written responses including audiovisual recordings if the adults agree prospectively

- **Benign behavioral intervention**
  - ✓ Brief in duration,
  - ✓ Harmless, painless, not physically invasive, no long adverse impact, AND
  - ✓ Researcher has no reason to think the subjects will find the interventions offensive or embarrassing
- Prospective agreement  (does not equal) [45 CFR 46.116](#) requirements for informed consent

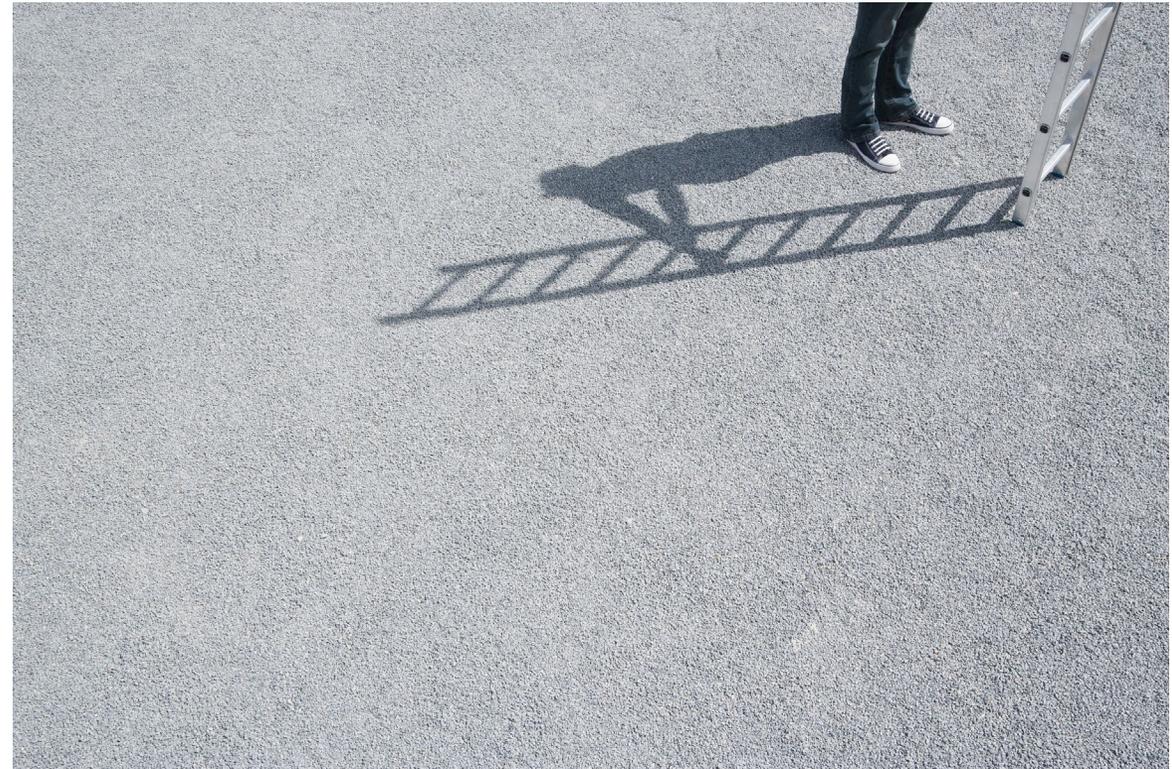


## Exemption 3 (CONT.)

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Exemption 3 allows for research that involves deception:

- The subject authorizes to be deceived regarding the nature or purposes of the research through a **prospective agreement** to participate in such a study



## Exemption 3: Example 1

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Adult subjects are asked to complete two games of “Sudoku” in a quiet room and then two games in a room with a white noise machine. Participants are briefly interviewed afterwards to learn if the white noise had any effect on completing the puzzles.

- Is the activity a “benign behavioral intervention”?
    - ✓ Is it brief in duration? ✓ (Yes)
    - ✓ Is it harmless, painless, not physically invasive, no long adverse impact? ✓ (Yes) AND
    - ✓ The researcher has no reason to think the subjects will find the interventions offensive or embarrassing? ✓ (Yes)
  - Is there a permissible form of data collection? ✓ (Yes)
  - Prospective agreement? ✓ (Yes)
  - Can the identity be not readily ascertained? ? (Not sure)
  - Would disclosure of the participants’ time not place them at risk? ✓ (Yes)
- **Yes, exemption 3 would probably apply**



## Exemption 3: Examples 2 & 3

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A researcher asks adults to play a computer “matching objects” game for 30 minutes with a timer that counts down. Participants’ eye movements are video-recorded to determine if there is a correlation between the speed in which they search the screen and amount of time left to complete the game.

- Benign behavioral intervention with a permissible form of data collection ✓ (Yes)
- Would disclosure of the participants’ times not place them at risk? ✓ (Yes)

### ➤ **Yes, exemption 3 would probably apply**

The researcher attaches a heart monitor to participants to record activity throughout the task.

- Is this a permissible form of data collection? ✗ (No)

### ➤ **No, exemption 3 would not apply**



## Exemption 3: Example 4

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Adult subjects are asked to be interviewed after watching a 30-minute video about clinical trials to determine if it influences their feelings about clinical research. In reality, however, the researcher is recording the participants to study their behaviors as he lowers the temperature throughout the video. Responses will be recorded with identifiers.

- Is disclosure likely to cause hardship? ✓ (Yes)
- Is the deception authorized? ✗ (No)

➤ **No, exemption 3 would not apply**



## Exemption 4 at §46.104(d)(4)

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Exemption 4 is for secondary research uses of identifiable private information or identifiable biospecimens

- Secondary research uses information or specimens collected for a different purpose other than the current research
- Identifiable indicates that the identity of the subject is or may readily be ascertained by the investigator or associated with the information or biospecimens



## Exemption 4 (CONT.)

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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, or
- ii. Information, 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, or



## Exemption 4 (CONT.)

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

- iii. Researcher's use of identifiable health information is when HIPAA applies for purposes of "health care operations" or "research" or for "public health activities and purposes", (**ONLY for INFORMATION, NOT BIOSPECIMENS**), or
- iv. Research is conducted by, or on behalf of, a federal department or agency using government-generated or government-collected information obtained for nonresearch activities and federal privacy regulations will apply

[Luminaries Lecture on HIPAA exemption 46.104\(d\)\(4\)\(iii\)](#)

(emphasis added)



## Exemption 4: Example 1

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An oncology researcher stores blood samples with identifiable information from previous clinical trials. In a new study, she wants to look for a link between prostate cancer and high levels of nickel in the bloodstream.

To test this hypothesis, she has her assistant pull 100 random blood samples, without any information. The assistant does not maintain a participant log.

- Is this secondary research? ✓ (Yes)
  - Is the information recorded in a manner that the samples are not identifiable? ✓ (Yes)
  - Will the investigator not contact or re-identify the subjects? ? (Not sure)
- **This MAY qualify for exemption 4 if the researcher will not re-identify or contact**



## Exemption 4: Example 2

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An oncology researcher stores blood samples with identifiable information from previous clinical trials. In a new study, she wants to look for a link between prostate cancer and high levels of nickel in the bloodstream.

To test this hypothesis, she has her assistant pull 100 random blood samples but has her maintain a log. If a link is found, the researcher will direct a different study team member to contact those men to inquire as to their diets.

- Is the information recorded in a manner that the samples are not identifiable? **X** (No)

➤ **No, exemption 4 would not apply**



## Exemption 5 at §46.104(d)(5)

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Research that is designed to study, evaluate, improve, or otherwise examine public benefit or service programs that is conducted or funded by the federal government. This includes:

- 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
- Each federal department or agency conducting or supporting the research has to list these projects on a federal website prior to starting the research



## Exemption 6 at §46.104(d)(6)

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Taste and **food quality evaluation** and consumer acceptance studies:

- i. If **wholesome foods without additives** are consumed, or
- ii. If a food is consumed that contains a food ingredient at or **below the level** and for a use found to be **safe**, or agricultural chemical or environmental contaminant at or below the level found to be safe, by the FDA or approved by the EPA or the Food Safety and Inspection Service of the USDA.



## Exemption 6: Example 1

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A researcher is interested in knowing which brand of yogurt is liked the most by children so she can advise schools on which yogurt to include in school lunch programs. Researchers will enroll 500 students to taste and rate five brands of store-bought yogurts for their flavor.

- Does exemption 6 apply to children? ✓ (Yes)
- Is this a food evaluation? ✓ (Yes)
- Are the yogurts wholesome (i)? ? (Not sure)
- Is the yogurt “safe”(ii)? ✓ (Yes)

➤ **Yes, exemption 6 would apply**



## Exemption 6: Example 2

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A researcher wants to find out if how lunches taste at school impacts eating behavior at home. Children are asked to rate the taste of food they have at lunch and complete a survey of what they eat at home.

- Is this a study of taste and food quality evaluation? **X** (No)

➤ **No, exemption 6 would not apply**



# Exemption Decision Charts

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Check out our [decision charts!](#)  
They are extremely helpful in  
reviewing the exemption criteria!

[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?



# Contacts and Resources

- Contact us or submit your questions to [OHRP@hhs.gov](mailto:OHRP@hhs.gov)
- Visit OHRP website at [www.hhs.gov/ohrp](http://www.hhs.gov/ohrp), particularly our Online educational offerings under Education & Outreach
- [Mini-tutorials](#) on IRB memberships, voting, and reviews
- Take our free, five-part [Human Research Protection Training](#)
- Check out OHRP's [About Research Participation](#) informational resources for the public

