



Security, Privacy, and Ethical Issues in Database Research

THE UNIVERSITY OF TEXAS

**MD Anderson
Cancer Center**

Making Cancer History®

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Investigators' Responsibilities in Database Research

- Ethical responsibility to participants
- Engagement in human subjects research
- Conducting research while employed by a “covered entity”
- Contractual obligations under a Data Use Agreement

Investigators' Responsibilities in Database Research

- Ethical responsibility to participants
 - Belmont principles
 - Beneficence – Non-maleficence
 - Respect for persons
- Engagement in human subjects research
- Conducting research while employed by a “covered entity”
- Contractual obligations under a Data Use Agreement

Belmont Report Principles

Beneficence – Non-maleficence:

- **Maximize benefits** and **minimize harms** associated with research.
 - Research-related risks must be reasonable in light of expected benefits.
 - Risk of breach of confidentiality is less than the knowledge that can be derived from an important hypothesis and a well-designed study.
 - **No risk is reasonable for a fatally flawed study.**

Principles Belmont Report

Respect for Persons **Autonomy**

- Acknowledges the dignity and freedom of every person.
- Requires obtaining informed consent from research subjects or their legally authorized representatives

Investigators' Responsibilities in Database Research

- **Ethical responsibility to participants**
- **Engagement in human subjects research**
 - Code of Federal Regulations, Title 45 Part 46, the Common Rule
 - IRB Approval
 - Informed Consent or Waiver
 - Federal wide Assurance (FWA)
- **Conducting research while employed by a “covered entity”**
- **Contractual obligations under a Data Use Agreement**

45 CFR Part 46

45 CFR Part 46.109 IRB review of research.

"An IRB shall review and have authority to approve, require modification in (to secure approval), or disapprove all research activities covered by this policy*."

*Research involving human subjects

Informed Consent

45 CFR Part 46.116 General requirements for informed consent.

“Except as provided elsewhere by this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject’s legally authorized representative.”

Waiver of Informed Consent

45 CFR Part 46.116 An IRB may waive the requirements to obtain informed consent provided that the IRB finds and documents...

1. Research constitutes no more than minimal risk to the subjects **and**
2. Waiver or alteration will not adversely affect the rights and welfare of the subjects **and**
3. Research could not practicably be carried out without the waiver or alteration **and**
4. Subjects will be provided with additional pertinent information, where appropriate

Not permitted in FDA-regulated studies but may be appropriate in survey studies, and studies of banked samples and data

Waiver of Informed Consent Bloopers

Research could not practicably be carried out without the waiver or alteration

“I would have to talk to all the patients.”

“I don’t consent patients on the weekend.”

“Fellow is no longer available to assist.”

“Informed consent takes a lot of time and this study isn’t worth it.”

“Some of the patients might refuse.”

Investigators' Responsibilities in Database Research

- **Ethical responsibility to participants**
- **Engagement in human subjects research**
- **Conducting research while employed by a “covered entity”**
 - **HIPAA Privacy Rule**
 - Authorization or Waiver
 - De-identification or Limited Data Set
 - Data Security (with encryption) of PHI
- **Contractual obligations under a Data Use Agreement**

Covered entity can use or disclose PHI if it...

- Obtains the individual's **Authorization** to use or disclose PHI
- Documents **IRB Waiver of Authorization**
- Obtains IRB approval for Alteration of Authorization and the individual's authorization
- Uses or discloses PHI for **activities preparatory to research**
- Uses or discloses PHI for **research on decedents**
- Uses or discloses a **limited data set** and enters into a **data use agreement**
- Uses or discloses information **stripped of 18 identifiers**
- Uses or discloses PHI based on informed consent (or waiver of same) prior to April 14, 2003

Waiver of Authorization

IRB must find and document that **all** of the following are true.

1. Research constitutes no more than minimal risk to the privacy of the subjects based on
 - An adequate plan to protect identifiers and data,
 - An adequate plan to destroy identifiers at earliest opportunity consistent with the research, **and**
 - Written assurance that PHI will not be reused or disclosed for any other purpose
2. Research could not practicably be carried out without the waiver or alteration
3. Research could not be carried out without access to the PHI.

**Key
Elements
of a Data
Security
Plan**

Waiver of Authorization Bloopers

Research could not practicably be carried out without the waiver or alteration

“It takes too much time.”

“My chairman will not give me a research nurse.”

“Many of the patients speak a foreign language and I can't talk to them.”

“Some of the patients are difficult to contact because they are dead.”

18 Items for De-Identification

Individuals, Relatives, Employers, or Household members

- Names
- Geographic subdivisions smaller than state, except first 3 digits of Zip
- All elements of dates except year. All ages over 89.
- Telephone numbers
- Fax numbers
- Email address
- Social security number
- Medical record number
- Health plan beneficiary number
- Account number
- Certificate or license number
- Vehicle & license plate number
- Device identifier & serial number
- URLs
- IP Address
- Biometric identifiers
- Full face photo
- Unique identifying code, except for re-identification

16 Items for Limited Data Set

Individuals, Relatives, Employers, or Household members

- Names
- Postal Address except city, state and Zip
- Telephone numbers
- Fax numbers
- Email address
- Social security number
- Medical record number
- Health plan beneficiary number
- Account number
- Certificate or license number
- Vehicle & license plate number
- Device identifier & serial number
- URLs
- IP Address
- Biometric identifiers
- Full face photos

Investigators' Responsibilities in Database Research

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Example of Data Use Agreement

- You will not use the data for purposes other than described in the memorandum.
- You will not permit others to use the data except for collaborators within your institution involved with the work as described in the memorandum. Within your institution or organization, access to the data shall be limited to the minimum number of individuals necessary to achieve the purpose stated in your proposal. For specific research projects, you will submit a brief proposal describing the analysis, the researchers involved and the data management for the particular project.

**Key
Elements
of a Data
Security
Plan**

Example of Data Use Agreement

- You will establish and maintain the appropriate administrative, technical, and physical safeguards to protect the confidentiality of the data and to prevent unauthorized use or access to it, as described below:

- *All servers that house the data and backup files will be located in secured, locked offices. U.T. MD Anderson is a policed campus. The servers are located in the MDACC Data Center in the Cancer Prevention Bldg. Access to the servers is protected by firewalls, and all accounts are password protected. Access to the data on the server will be limited to researchers involved in the project. DVDs with the original data will be stored in a locked file cabinet in the Principal Investigator's office, Room FCT 4.6008, in Pickens Tower Bldg at MD Anderson.*

**Key
Elements
of a Data
Security
Plan**

Example of Data Use Agreement

- If you move to a different institution, you will contact NCI in writing PRIOR to moving for instructions on how to handle the data. You may not duplicate any files prior to moving nor can you take data with you without written permission from NCI.
- No findings or information derived from the data may be released if such findings contain any combination of data elements that might allow the deduction of a patient's or any providers' identity. In tables, cell sizes less than 11 (eleven) must be suppressed. You agree that NCI shall be the sole judge as to whether any finding derived from the data would, with reasonable effort, permit one to identify an individual or provider, or to deduce the identity of an individual or provider to a reasonable degree of certainty.

Example of Data Use Agreement

Key Elements of a Data Security Plan

- You agree that in the event NCI determines or has a reasonable belief that you have violated any terms of this agreement, NCI may request that you return the data and all derivative files to NCI. You understand that as a result of NCI's determination or reasonable belief that a violation of this agreement has taken place, NCI may refuse to release further data to you for a period of time to be determined by NCI.
- All files received may be retained for a maximum of five years. At the completion of the project or five years from receipt all files must be destroyed and notification of destruction must be sent to NCI. Investigators who need to retain files beyond that period must contact NCI.

*Still have the courage to do
research?*

Getting started

- “Activities or review prior to research” can be done without prior approval from IRB. The activities include queries of data, without recording identifiers, or obtaining aggregated data from a data custodian in order to demonstrate a project’s feasibility or design the study. PHI reviewed for this purpose cannot be removed from the covered entity and cannot be published.

Are you doing human subjects research?

- Research is the collection and aggregation of data that permits conclusions to be drawn, and develops or contributes to generalizable knowledge.
- Research may involve direct interactions with living individuals or indirect activities.
- Quality improvement is the collection and aggregation of data to improve quality of care or operations in a single institution/entity. There is no plan to generalize to other settings.

Are you doing human subjects research?

- *45 CFR 46.102 (f) 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.
- *Private information* includes
 - information about a behavior that occurs in a context that an individual can reasonably expect that no observation or recording is taking place, and
 - Information provided for specific purposes that the individual can reasonably expect will not be made public (i.e a medical record)

Are you doing human subjects research?

- *Private information* must be **individually identifiable** (the identity of the subject is or may readily be ascertained by the investigator or associated with the information) in order for obtaining the information to constitute human subjects research.
- *Private information* is not considered individually identifiable if it cannot be linked to specific individuals by the investigator either directly or indirectly through coding systems.

Are you doing human subjects research?

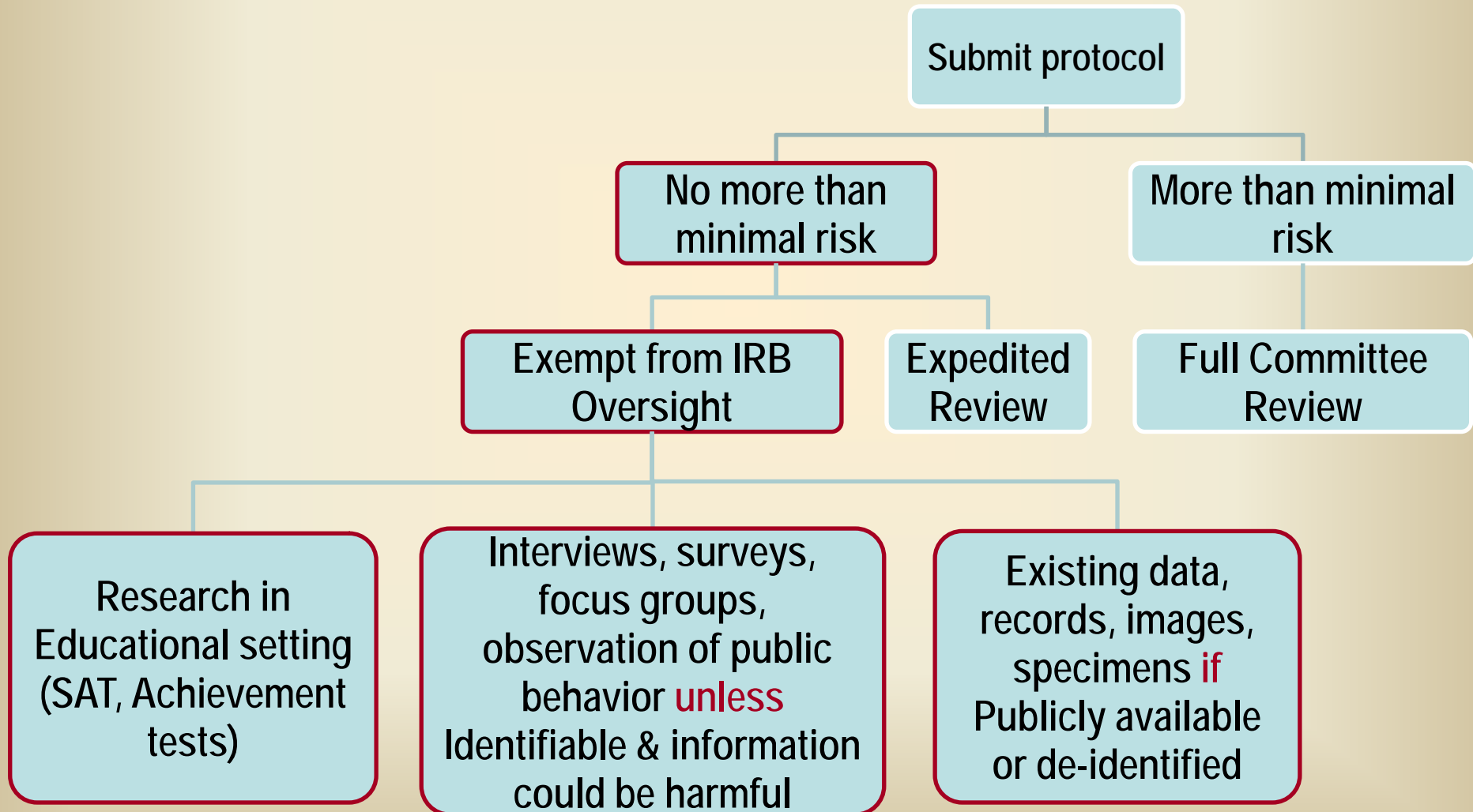
- OHRP does not consider research involving coded information to involve human subjects if both of the following conditions are met:
 - The data were not collected specifically for the currently proposed research through an interaction or intervention with living individuals; **and**
 - The investigators cannot readily ascertain the identity of the individuals because, for example:
 - The investigators and the holder of the key enter into an agreement prohibiting the release of the key to the investigators under any circumstances; **or**
 - There are IRB approved written policies for a repository that prohibit the release of the key to the investigators under any circumstances; **or**
 - There are other legal requirements prohibiting the release of the key to the investigator until the individuals are deceased.

Submit your protocol for IRB review.

IRB's Responsibilities – Database Studies

- Risk to subjects are minimized
- Evaluating risks (harms) vs. benefits – loss of confidentiality vs scientific validity
- Selection of subjects equitable – studies produce valuable information about all those affected, and all those who may benefit share equitably in the risks
- Informed consent (and assent) - sought from each subject or legal representative, unless waived
- Monitoring data collected to ensure safety and ethical treatment of subjects
- Protect privacy and confidentiality of subjects
- Safeguard welfare of vulnerable groups

IRB Decision Making



Exempt Research

- Educational tests, (cognitive, diagnostic, aptitude, achievement)
- Surveys, focus groups, interviews or observation of public behavior, **unless** –
 - 1) subjects can be identified

and

 - 2) disclosure of the responses could be harmful

Exempt Research

- Collection or study of available data, documents, records, pathological specimens, or diagnostic specimens, **if** –
 - 1) sources are publicly available

or

 - 2) subjects cannot be identified

Exempt Research

- Exempt status must be determined by the IRB – not the PI
- Exemption from IRB review does **NOT** relieve PI of responsibility for obtaining informed consent and authorization or obtaining waivers of same

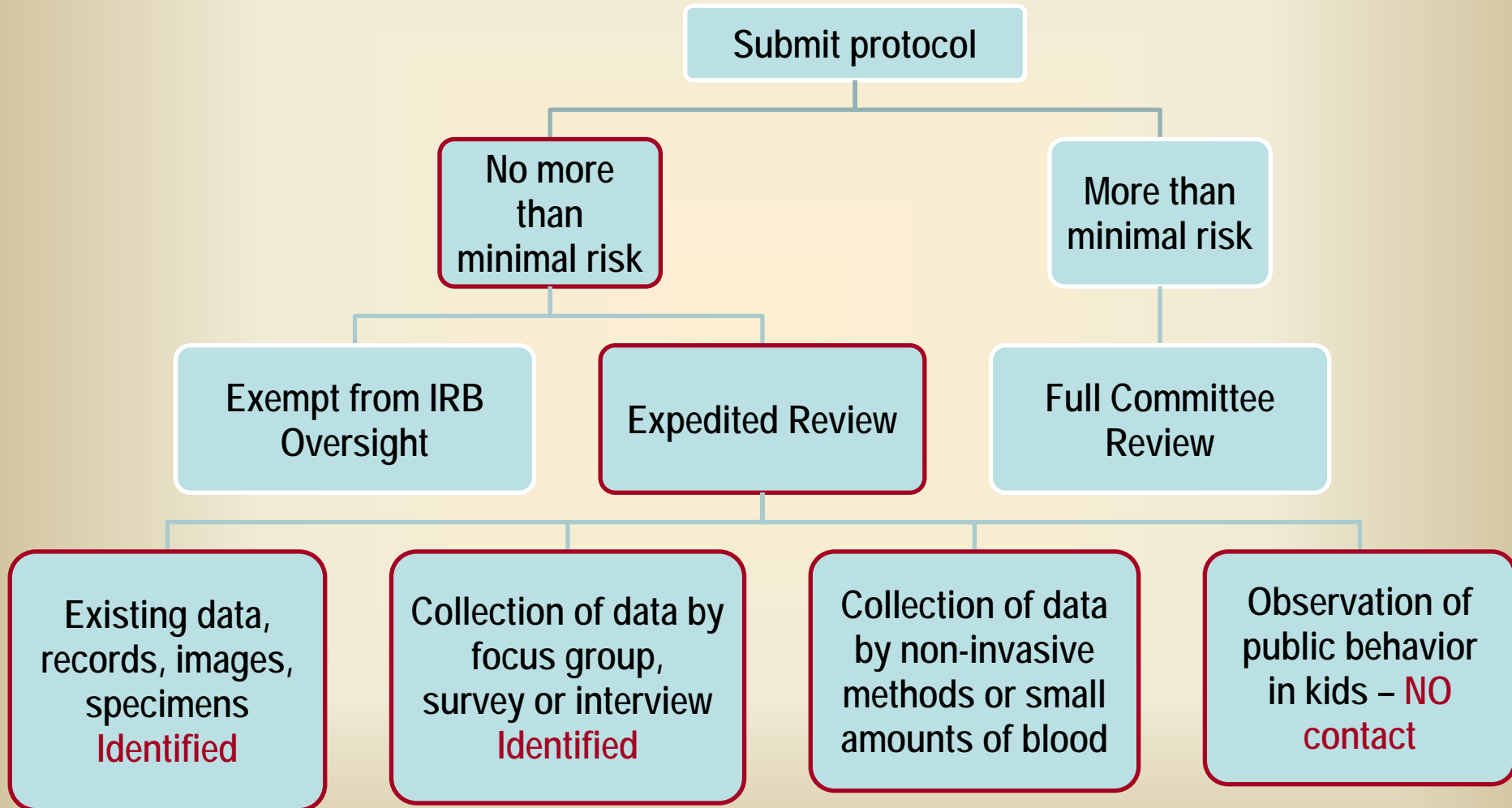
Examples of Exempt Research

- Use of SEER database or claims databases – de-identified and publicly available
- Interviews that **do not** involve protected health information or information that could place patients at risk of civil or criminal liability or be damaging to subjects' financial standing, employability or reputation. (Opinion surveys, focus groups)
- Interviews involving protected health information that are de-identified (BRFSS, NHIS) Anonymous internet surveys
- Examination of de-identified clinical data, films, images, or samples

Exempt Research

- Exemption is determined by the IRB – not the Investigator
- Exemption from IRB Oversight \neq Exemption from Obtaining Informed Consent
 - Obtain Informed consent or request and justify a **Waiver** for all human subjects database research
- Exemption from IRB Oversight \neq Exemption from Obtaining Authorization
 - Obtain authorization or request and justify a **Waiver** for all research involving protected health information, even if not considered human subjects research by IRB. Exceptions: deidentified or limited data set with a DUA

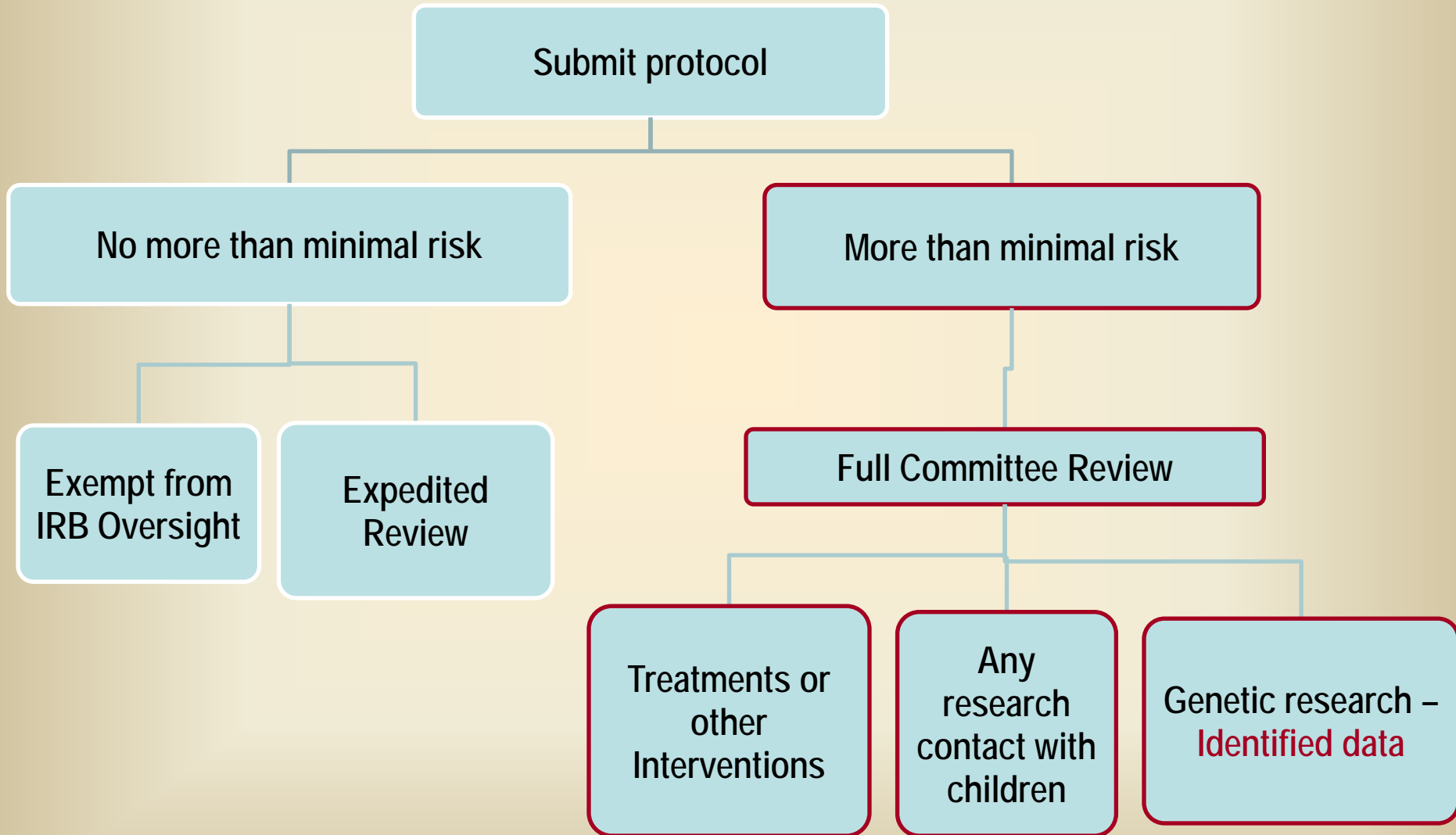
IRB Decision Making



Examples of Research Eligible for Expedited Review

- Surveys, interviews, or focus groups collecting **identifiable**, protected health information or information that could be damaging to a person
- Examination of **identifiable** clinical data, films, images, or samples
- Studies that involve collection of small amounts of blood, etc
- Observational studies in children, prisoners, and other vulnerable populations (i.e. employees, students)

IRB Decision Making



Parting Tidbits

Possession \neq Permission

Data obtained for a prior study cannot be used for other purposes without specific IRB approval.

Data in databases cannot be used without IRB approved protocol for specific use.

Low Risk \neq Low Quality

No risk is justifiable for a fatally flawed study. Develop database research protocols with the same careful attention to scientific rigor as clinical trials.

Exemption from IRB Review \neq Exemption from Consent and Authorization

Request and justify waivers.

Parting Tidbits

Every database study that you conduct should have ...

- Important hypothesis
- Excellent study design & analytical plan
- Thorough data security plan
- IRB approval, exemption, or a memo from IRB stating it is not human subjects research.
- Signed &/or documented Informed Consent or a waiver from IRB unless not human subjects research
- Signed &/or documented Authorization or a waiver from IRB – even if IRB determines that the research is not human subjects research. Exceptions: deidentified data set or limited data set with a DUA



Office for Human Research Protections (OHRP)

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- [IRB Workshop Summary November 2005](#)
- National Conference on Alternative IRB Models November 2006
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- [Questions to Ask](#)

[Regulations and Policy Guidance](#)

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- [Expedited Review Categories](#)
- [Guidance By Topic](#)
- [Decision Charts](#)
- [Belmont Report](#)
- [Related Resources](#)
- [OHRP Correspondence](#)

[Educational Resources/QI](#)

[Conferences](#)

- [Quality Improvement Consultations](#)
- [Educational Materials](#)
- [Online Training](#)

[Requests for Public Comment](#)

[Secretary's Advisory Committee \(SACHRP\)](#)

[Charter](#)

- [Members](#)
- [Meetings](#)
- [Contact](#)

[About OHRP](#)

[Mission](#)

- [Organizational/Structure](#)
- [Organizational Chart](#)
- [Staff Listing](#)
- [Contact Information](#)
- [Visitor Information](#)
- [FOIA Requests](#)

Policy Guidance [by topics]

Guidance Topics

<http://www.hhs.gov/ohrp/policy/index.html#topics>

- [407 Review Process](#)
- [Adverse Events](#) (see also Unanticipated Problems)
- [AIDS](#)
- [Assurance FAQs](#)
- [Biological Specimens](#) (see also Coded Private Information)
- [Children](#)
- [Certificate of Confidentiality](#)
- [Clinical Trial Websites](#) (see also IRBs)
- [Coded Private Information](#) (see also Biological Specimens)
- [Common Rule](#)
- [Compliance Oversight](#)
- [Conflict of Interest](#)
- [Consent](#) (see also [Informed Consent](#))
- [Continuing Review](#)
- [Databases and Data Storage](#)
- [Decision Charts](#)
- [Emergency Research](#)
- [Engagement in Research](#)
- [Exculpatory Language](#)
- [Exempt Research/Exemptions](#)
- [Expedited Review](#)
- [Fetal Tissue](#)
- [Frequently Asked Questions \(FAQs\)](#)
- [FWA](#)
- [Genetic Information Nondiscrimination Act \(GINA\)](#)
- [HHS Funding/Support](#)
- [HIV/AIDS](#)
- [Human Subjects](#)
- [Incident Reporting](#)
- [Individual Investigator Agreement](#)
- [Informed Consent](#)
- [Informed Consent FAQ's](#)
- [Investigator Responsibilities FAQs](#)
- [In Vitro Medical Devices](#)
- [IRBs](#)
- [IRB Registration FAQs](#)
- [Pharmaceutical Companies](#)
- [Prisoners](#)
- [Quality Improvement Activities](#)
- [Research](#)
- [Repositories](#) (see also [Tissue Storage/Repositories](#))
- [Stem Cells](#)
- [Tissue Storage/Repositories](#)
- [Unanticipated Problems](#) (see also Adverse Events)

Questions??