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Association for the Accreditation of Human Research Protection Programs, Inc. — Full Accreditation

Secondary Analysis of Existing Data and Samples

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Secondary Analysis

Secondary analysis of existing data and samples make up a substantial portion of all research at CHLA.

- Ideal research entry point for students, residents, fellows, and first time PIs
- Foundation for more complex projects.

This presentation will walk you through the major decision points of study design and provide tips to simplify the approval process.

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Deciding What You Need From Your Research

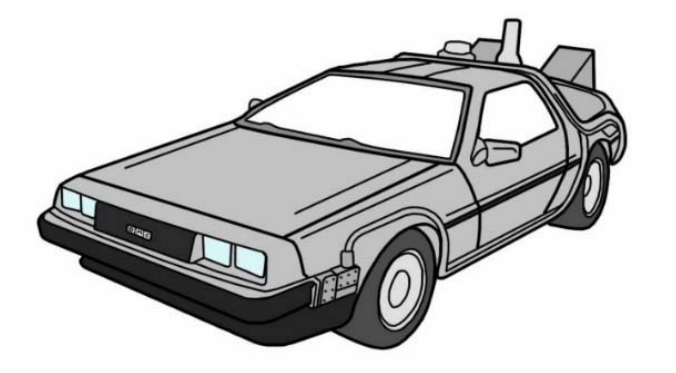
With some forethought about what you do and don't need for your project informing:

- What you collect
- When you collect
- How you collect it

You can simplify the IRB approval process.

Retrospective vs. Prospective

For research purposes, **Retrospective** – *Data or samples that exists at the time of your initial IRB Submission.*



If all the data and samples you need exist at the time you submit your IRB application, congratulations! You're doing retrospective research aka secondary research on existing data or samples. This is the simplest path to approval.

Retrospective vs. Prospective

In research as in life, patience is a virtue.

If all the data and or samples you need have not yet been collected, will they be if you wait a little while?

If the answer is yes, you can make your life easier by waiting to start your research until everything you need has been collected.

Once they've all been collected, your research can be considered **retrospective**.

Retrospective vs. Prospective

With the new common rule, it also possible to have data collected prospectively, as long as it is not collected specifically for the research.

So it is possible to do a prospective chart review study as long as the data you need is being collected as a part of normal care.

Deciding What Type of Application to Submit

There are 3 types of applications for research involving secondary analysis of existing data and specimens

- Coded Data/Non-Human Subjects Research
- Exempt
- Expedited

Knowing the differences and which best fits your needs is difference between a 6 and a 26 page application.

What Type of Application to Submit - NHS

Coded Data/Specimens (Non-Human Subjects Research) is the shortest application and doesn't require annual renewal. The two relevant regulatory definitions for this research are

45.46.102 (I) which defines **Research** as:

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

Non Human Subjects Research

And 45.46.102 (e)(1) which defines **Human Subjects** as:

A living individual about whom an investigator 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*

Non Human Subjects Research

For NHS review, you must not have contact with your subjects and you must not be able to identify them through their information/samples. This usually means material collected by someone else that is either anonymous to start with, or will be anonymized before you receive it.

Some examples include:

- Material from a publically or commercially available source
- Material that was collected without identifiers to start with

Non Human Subjects Research

If your research materials meet these requirements, then CHLA's simplest application, coded data/specimens is the way to go. The advantages of this type of determination are:

- No human subjects = no requirement for consent
- One time approval, no requirement for annual review

What Type of Application to Submit – Exempt

If your materials don't qualify for Non Human Subjects research, the next option is an **Exemption.**

The Exempt application is a little longer, but it's still relatively painless.

For secondary review of existing data and samples, exemption 4 is your ticket. Until the revisions to the common rule that went in effect in January of this year, there were restrictions on this exemption that limited you to de-identified data.

Exempt

The revised exemption is much more useful. There are now 4 categories of research that can be approved under this exemption

(i) The identifiable private information or identifiable biospecimens are publicly available;

This is very similar to the old exemption and NHS, the difference is that the data/samples can be identifiable.

I've yet to see this one in action.

Exempt

(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;

Also very similar the old exemption 4.

Notice the emphasis on "cannot readily be ascertained" identifiers that can be included are the traditional limited dataset items: dates, city, state, zip, ages in years, months, dates

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Exempt

You can use data/samples as long as you don't contact or re-identify your subjects.

Also, the key code document can be used to during creation of you data set, but needs to be destroyed it prior to study analysis.

Exempt

(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

This is the gamechanger. It allows you to collect **identifiable** data, provided that it is covered by the HIPAA Privacy Rule

Research HIPAA Authorization

Is it applicable? Will you be reviewing:

1. Names
2. Address including city and zip code
3. Elements of dates
4. Phone numbers
5. Fax numbers
6. Electronic mail addresses
7. Social Security numbers
8. Medical record numbers
9. Health plan beneficiary numbers
10. Account numbers
11. Certificate/license numbers
12. Vehicle identifiers and serial numbers
13. Device identifiers and serial numbers
14. Web Universal Resource Locators (URLs)
15. Internet Protocol (IP) address numbers
16. Biometric identifiers, including finger and voice prints
17. Full face photographic images and any comparable images
18. Any other unique identifying number, characteristic, or code

Exempt

This allows the IRB to exempt chart review research that previously required expedited category 5.

- Cannot be used for secondary analysis of biospecimens
- Cannot be used for secondary analysis of research datasets

The advantages of the exemption are:

- Consent is not required for exempt research, so there is no need to justify a waiver.
- One time review, no annual review is required.

Exempt

Lastly,

(iv) The research is conducted by, or on behalf of, a Federal department or agency using government-generated or government-collected information obtained for nonresearch 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…

The use case for one is pretty limited, so I haven't seen it in action yet.

What Type of Application to Submit - Expedited

The last application type for secondary research is **Expedited.** Specifically:

Category 5, *Research involving materials (data, documents, records, or specimens) that have been collected, or will be collected solely for nonresearch purposes (such as medical treatment or diagnosis).*

We used to do a ton of these applications, but now that exempt 4 data can be identifiable, the main advantage of category 5 is gone. Standalone category 5 chart reviews are an endangered species.

Expedited

Category 5 can still be used if you are:

- Doing secondary analysis of biospecimens
- Doing secondary analysis of research datasets or other data sources that are not protected by HIPAA

It's also still used if you are including a chart review component in a larger expedited project with a drug, device or intervention.

Minimum Necessary Principle

Since it can directly impact the type of application you submit, now is a good time to consider the minimum necessary principle of research.

The idea that you should only collect the minimum necessary information required to answer your research question should be kept in mind when selecting the variables you need to collect.

For example if you're collecting DOB, would subject age capture the same information while minimizing the risk of a subject being identified?

Data Collection Sheets Tips

We will request a data collection sheet regardless of the review type

- Whenever possible, submit a copy of the actual sheet you will be using to collect your data
- If you can explain what is being collected on the data sheet, it speeds up the process
- Never send us subject data
- Think about how dates are being collected

New Protocol Templates

In the coming weeks, the HSPP will be rolling out a series of new protocol template documents that will help you to answer questions that staff and reviewer may have about your study.

The first to be released will be a chart review template that will help you to navigate the important decision points of your project.

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Subject Consent

The nature of secondary research often means that you can't consent subjects or it isn't necessary because what you are dealing with is de-identified data and not a person. However, it's very likely that if the data was collected properly in first place, subjects consented to your use of their data or samples. So even when you can't see it, consenting is still a part of research.

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Subject Consent

As previously discussed, for your non human subjects or exempt research, consent is not required.

Expedited research requires either consent or a waiver of consent.

A **waiver of consent** is appropriate only if the research would not be practicable without it.

- Subjects lost to follow-up or otherwise not available to provide consent.
- Large number of subjects (100 or more)

Research HIPAA Authorization

If you are using any information HIPAA privacy act for your research or accessing records to identify subjects, then you need to address HIPAA.

1. Much like with consent, you should get authorization when you can.
2. If you can't consent subjects because they are lost to follow-up or too numerous, a waiver of authorization is available.

Research HIPAA Authorization

- The nature of NHS research means that HIPAA won't come into play.
- Exempt 4(III) will require a waiver of authorization.
- Similarly, most expedited chart reviews will require waivers of authorization.

Research HIPAA Authorization

- Waivers of Authorization cannot be granted retroactively, so it is important to understand your HIPAA obligation up front.
- If you have questions, ask us **before** you collect your data.
- Failure to address HIPAA can force you to either go back and contact all of your subjects or discard your data.

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De-Identified vs. Coded Data

These are the two most commonly confused terms in research. First, they are not interchangeable, they are two different things. The confusion however, is somewhat understandable because depending on how you handle it, coded data can become de-identified. If you code your study data, it is **NOT** de-identified as long as the key to code exists. Even if you send coded data to an outside collaborator, it is still coded as long as the key exists.

De-Identified vs. Coded Data

Your collaborator can still come back to you and say, “I need more information on subject 001.”

If on the other hand you strip the study ID column out of your data and send it without any identifiers at all. Then the data is actually de-identified. Once the key has been destroyed, the data is anonymous

If this still doesn’t make sense to you, don’t worry. We will ask the questions to get to the bottom of it with you.

What Type of Application to Submit

This presentation has covered the broad strokes, but if you are having some difficulty determining which application or consent approach fits your project, DHHS has created a suite of flow charts to guide you through the decision-making process:

https://www.hhs.gov/ohrp/sites/default/files/full-2016-decision-charts.pdf

Questions

Any Questions about this presentation, your IRB application or approval, please call us any time.

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