Human Subjects Committee Guidelines

These guidelines are intended to assist investigations and ASRS Human Subjects Committee reviewers in their evaluation of whether scholarly activities are subject to IRB oversight per U.S. federal regulatory standards. Scholarly activities that are subject to IRB oversight and did not receive it cannot be accepted for presentation or publication by ASRS.

Introduction: Evaluation of whether an activity is subject to IRB approval under U.S. federal regulatory standards involves a series of determinations including determining whether the activity is research, and, if so, whether the research involves human subjects per the regulatory definitions (See the **Important Definitions Guidance** for the full definitions and tips about their application).

Scholarly activities that are not research, or are research but do not involve human subjects, do not require IRB approval.

When a scholarly activity does involve human subjects research, reviewers should then evaluate whether the activity falls within one of the categories of research that federal regulators consider to be of such low risk that IRB approval and ongoing oversight is not required. Such human subjects research is described in the regulations as "exempt".

1. **Single Case Report**

   Case reports describing a single individual or case are generally not considered 'research' under U.S. federal regulatory standards because the scholarly activity does not involve a 'systematic investigation'.

   (NOTE: When a case report describes the use of an FDA-regulated (on or off label) drug, device, or biologic in a single patient, the case report itself is not typically subject to FDA regulations (unless the report is used to support an application to the FDA) and would not require IRB review.)

2. **Case Series of ≤ 10 cases**

   Case series of ≤ 10 cases are generally not considered 'research' under the U.S. Common Rule when they are descriptive in nature and do not include rigorous methods of analysis that are generally accepted as sufficient when establishing scientific evidence. Simple mathematical descriptors (e.g., percentages, numbers) are acceptable.

   Case series that include seeking out cases from outside one's own patients or practice begin to take on the appearance of a 'systematic investigation' but still may not meet the regulatory definition of 'research' as long as they are not 'designed to develop or contribute to generalizable knowledge'.

   (NOTE: Case series of ≤ 10 cases that do meet the Common Rule definition of research may qualify for exempt status under Category 4 if all conditions of the exemption are satisfied.)

3. **Literature Review**

   Literature reviews that do not include any review or use of individual level data (e.g., for data validation) are generally excluded from the requirement for IRB review because the activity does not involve 'human subjects' as defined by the U.S Common Rule.

   (NOTE: Literature reviews that do include the use of individual level data may still qualify as 'not human subjects' when the identities of the individuals are not known to or able to be readily ascertained by the

investigator(s). When a literature review does involve human subjects, reviewers should consider whether the literature review would qualify for exempt status under Category 4.)

4. Meta-analysis

As with literature reviews, meta-analyses that do not include any review or use of individual-level data are generally excluded from the requirement for IRB review because the activity does not involve 'human subjects' as defined by the Common Rule.

(NOTE: Meta-analysis methods that do include the review and use of individual-level data (e.g., for pooled analyses) may involve 'human subjects' when the data is identifiable, or coded and re-identification is reasonably possible (e.g., because the investigator(s) has access to the code, or the data may become readily identifiable as a result of the pooling of data). When a meta-analysis does involve human subjects, reviewers should consider whether the analysis would qualify for exempt status under Category 4.)

5. Analysis of registry data (e.g., Vestrum, IRIS, or another large-scale professional database)

Much research utilizing data from a large-scale professional database can be excluded from the requirement for IRB review because the research does not involve 'human subjects' as defined by the Common Rule. Common examples of this include:

- When the data provided to the investigator is in aggregate form
- When the dataset provided to the investigator is large and has been stripped of all identifying information, and the investigator does not have the means to readily re-identify subjects because they do not have direct access to the database, do not have access to any coding system that would enable re-identification, and, ideally, there are terms of use or an agreement that prohibits re-identification.

(NOTE: When the investigator is conducting research using a small dataset (e.g., only patients with a rare diagnosis), or only using the data from their own practice that has been submitted to the database, the research may involve human subjects because the investigator knows, or may readily ascertain, the identities of at least some subjects. In such cases, reviewers should consider whether the research qualifies for exempt status under Category 4.)

6. Retrospective Chart Review (other than single case report or ≤ 10 case series)

Many retrospective chart reviews that are 'human subjects research' qualify for exemption under Category 4, sub-criterion (iii) (for information protected by HIPAA). For this exemption to apply, any data including protected health information must remain appropriately secured within covered entities. This exemption could not be used when data is shared with collaborators who are not part of a covered entity unless the data has been de-identified in accordance with HIPAA standards or is covered by a business associate or data use agreement (for Limited Data Sets).

Retrospective chart reviews that only use data about patients outside of the investigator's practice may qualify as either:

- Not involving 'human subjects' research if the data is provided in a fully de-identified format and the investigator does not have the means to re-identify the information; or
- Eligible for exempt status under Category 4, sub-criterion (iii) (for information protected by HIPAA).

(NOTE: When investigators conduct research analyses using the data of patients from within their own practice, such activities almost always constitute 'human subjects research' as defined by the U.S. Common Rule because the investigators know, or can readily ascertain, the identities of the individuals associated

with the data. Exceptions to this general rule may exist for certain internal quality activities, when the intent of the activity is purely for quality improvement, the design and analysis use accepted QA/QI methodologies (versus the types of design and analyses more commonly associated with research intended to establish scientific evidence), and any subsequent publication or presentation is descriptive in nature.)

7. Other

a. Interviews, Surveys, Questionnaires

Studies that include the collection of data through interviews, surveys, questionnaires, or focus groups may qualify for exemption under Category 2 as long as the data is recorded without identifiers or is recorded with identifiers, but any release of the data wouldn't be harmful (see Category 2 Reviewer Tips in the Reviewer Checklist for more information).

b. Prospective Data Collection

Studies that include prospective data collection may qualify for exemption under Category 4 as long as the data is being generated for another 'primary' purpose (e.g., provision of health care) and at least one of the sub-criteria is satisfied (publicly available data, data recorded without identifiers, or data protected under HIPAA). (See Category 4 Reviewer Tips in the Reviewer Checklist for more information).

c. Public Datasets

Studies that involve the use of data available to any member of the public may qualify as either "not human subjects" or qualify for exemption under Category 4. To differentiate, first determine whether the data is "identifiable private information" using the definitions in the Important Definitions Guidance. Research involving public data that is not identifiable and/or not private does not involve human subjects per the Common Rule and does not have to be evaluated to determine if it qualifies for exempt status. When the data is available to the public, and is both identifiable and private (e.g., a public health dataset that could be re-identified by comparing it with other data or through the use of an algorithm), then the research should be evaluated for potential exemption under Category 4.

d. Education

Studies that involve the evaluation of educational strategies (e.g., provision of information to patients in a video versus a handout combined with a post-test to evaluate understanding) should be considered for exemption under Category 1. Category 1 should not be applied to research using novel educational strategies, a condition of the exemption is that the research only involves normal educational practices.

Studies that involve the use of educational tests, or the results of educational tests, may be considered for exemption under Category 2. Unlike Category 1, Category 2 may not be used when the research includes any sort of 'intervention' such as an educational strategy or manipulation of circumstances.