must meet the requirements for prior submission to the Food and Drug Administration under section 505(i) or 520(g) of the act, or need not meet the requirements for prior submission to the Food and Drug Administration under these sections of the act, but the results of which are intended to be later submitted to, or held for inspection by, the Food and Drug Administration as part of an application for a research or marketing permit.

Intended
Likely to be; plan to

Involves
The prospective physical use of a test article in a way that is not completely up to the discretion of a clinical practitioner.

Premarket Review
Review of any of the following: investigational new drug (IND) application, investigational device exemption (IDE), humanitarian device exemption (HDE), new drug application (NDA), biologics license application, device premarket notification (510K notification), device reclassification petition, or premarket approval application (PMA).

Research or Marketing Permit
Same as premarket review

Test article
Any product that is regulated by the Food and Drug Administration, including:

- Foods
- Dietary supplements
- Infant formulas
- Food and color additives
- Drugs for human use
- Medical devices for human use
- Biological products for human use
- Certain electronic products used for human health care

See the HSD Glossary for the definitions of drug, device, and biologic.
Note that some software and mobile medical devices are regulated by the FDA.

EXAMPLES
The UW believes that the following activities are not subject to FDA regulations:

- Medical records review (retrospective or prospective)
- Use of a medical device when the purpose is to obtain basic physiological information
- Studies of surgical techniques that are evaluating only a new technique and not the safety or efficacy of an FDA-regulated item
- Use of a custom device, if it is not being used to gather safety or efficacy data that will be submitted to the FDA
- Activities that meet the FDA's definition of being exempt from FDA regulations
- When the sole activity(s) of UW employees or agents on an FDA-regulated study conducted by a non-UW PI is limited to:
    - Data analysis (whether or not the data are identifiable)
    - Accessing and providing medical records of participants
    - Recruiting activities prior to obtaining consent
    - Pre-screening of records for eligibility determination
    - Procedures that are to be performed as part of clinical practice and which would be performed exactly the same way regardless of whether study entry was contemplated, such as diagnosis or treatment of a disease or medical condition

REGULATORY REFERENCES

- 45 CFR 46.102
- 21 CFR 50.3; 21 CFR 56.102; 21 CFR 312.3; 21 CFR 812.3
- OHRP "Guidance on Research Involving Coded Private Information or Biological Specimens", October 16, 2008.
- FDA "Guidance on Informed Consent for *In Vitro* Diagnostic Device Studies using Leftover Human Specimens that are Not Individually Identifiable", April 25, 2006.

END NOTES

human subjects definition of "identifiable".

Some specific circumstances in which the information would not be considered identifiable:

- *The identifiers or the key to the identifier code have been destroyed.*
- *The research team has entered into an agreement with the holder of the identifiers or code key that prohibits the release of the identifiers or code key to the team members.*
- *When the data come from a repository or data management center: There are IRB-approved written policies and procedures for the repository or center that prohibit the release of the key to the team members.*
- *There are other legal requirements prohibiting the release of the identifiers or code key to the team members.*

Conclusion

If both boxes are checked: human subjects are involved, as defined by the Common Rule. Proceed to Part 6 to see if the research is subject to FDA regulations.

If one or no box is checked: human subjects are not involved, as defined by the Common Rule. Proceed to Part 6 to see if the research is subject to FDA regulations.

END PART FIVE

6. Human Subjects Research as Defined by the Food and Drug Administration

If an activity meets the FDA definition of human subjects research, then the activity must comply with the FDA regulations about informed consent (21 CFR 50) and IRB review (21 CFR 56). Final authority. The FDA has the ultimate authority on this issue. In the absence of any FDA opinion on a specific activity, it is UW policy that HSD staff make the determination about the applicability of specific FDA regulations, based on information provided by the researcher.

- The GUIDANCE: Applicability of FDA Regulations provides specific information about what this means.
- It does not necessarily mean that an Investigational New Drug (IND) approval or Investigational Device Exemption (IDE) is required from the FDA.
- If the activity does meet the FDA's definition of human subjects research, then the following WORKSHEETS can be used to help determine whether an IND or IDE is needed: WORKSHEET: FDA Drugs and the IND Requirement; WORKSHEET: FDA Devices and the IDE Requirement.

The FDA definition of research, and the UW interpretations of specific words in the definition, are provided in the Notes below. HSD has established the following criteria to use when deciding when an activity meets this definition.

Check if "**YES**".

☐ FDA definition of research. The activity is research if both of the following conditions are met:

- ☐ The intent of the activity is to develop information about the *test article* for submission to, or inspection by, the FDA in connection with any type of *premarket review* by the FDA.
- ☐ The activity involves the prospective physical use of a test article regulated by the FDA, in a way that is not completely up to the discretion of a clinical practitioner.

☐ FDA definition of human subject. Either or both of the following are true:

- ☐ The research involves a living individual who is or becomes a participant in research, either as a recipient of a test drug, device (including in vitro diagnostics) or biologic, or as a control. The individual may be either a healthy individual or a patient.
- ☒ An individual on whose specimen an investigational device or control is used in the research, even if the specimen is anonymous.

Conclusion

If both boxes are checked: the activity is human subjects research as defined by the FDA.

If no or one box is checked: the activity is not human subjects research as defined by the FDA.

END PART SIX

NOTES

DEFINITIONS

FDA Definition of Research (21 CFR 56.102(c))

Note that the FDA uses the following terms synonymously: clinical investigation, clinical study, clinical research, research, study and experiment. The UW interpretation of the underlined terms are provided in the definitions below.

Clinical investigation means that any experiment that involves a test article and one or more human subjects, and that either

The data are obtained through **interaction**.

Interaction: Communication or interpersonal contact between a member of the research team and the individual. Surveys - whether in-person, web-based, mail, email, phone, etc. - are an interaction between researchers and individuals.

*Obtain: Record in any fashion (writing, video, email, voice recording, etc.) for research purposes and retain for **any** length of time.*

☐ *This includes so-called "**third party**" or "**secondary subject**" situations in which researchers obtain information about one individual through interaction with another individual. Example: a researcher is studying married couples where one spouse is the primary caregiver for the other spouse who has Alzheimer's disease and who is living at home. When the caregiving spouse provides the researcher with individually-identifiable private information about the spouse with Alzheimer's as a required part of the protocol, then the spouse with Alzheimer's is a human subject.*

Note: Individuals who "screen out" of a study because an intervention or interaction (such as a screening phone call or lab test) reveals that they do not meet the study eligibility criteria are still considered human subjects if they meet all of the criteria outlined in this Worksheet.

Conclusion

If one or more boxes are checked: human subjects are involved, as defined by the Common Rule or other federal law. Proceed to Part 6 to see if the research is subject to FDA regulations.

If no boxes are checked: proceed to Part 5.

END PART FOUR

5. Human Subject as Defined by the Common Rule (45 CFR 46): Component 3

Check if "YES".

The data will be obtained about the individuals is **private** information.

Private information is defined as one or both of the following:

1. *Information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place.*
2. *Information which has been provided for specific purposes by an individual and which the individual can reasonably expect will not be made public (for example, a medical record or a residual medical specimen that is "leftover" from a health care procedure).*

☐ *Information: records, specimens, x-rays, photos, recordings and all other types of data*

Publicly available data are not considered private.

Any information about the individuals that is collected specifically for the proposed research project through an interaction or intervention with the individual by the investigator or other member of the research team is considered to be private.

If permission is required to obtain information, then the information is usually considered private. There are numerous "gray" areas in distinguishing "private" from "non-private". For example, there are some situations that are best considered "semi-private". This may include some behaviors, communications, and interactions that occur in electronic or social media. Also, a specific type of information may be considered private for one group of individuals but not for another.

The private information is **identifiable**.

Identifiable: The identity of the individual is or may readily be ascertained or associated with the information by a member of the research team, OR a member of the research team could readily identify the individual through a constellation of the data variables.

Research team: Anyone involved in conducting the research. The act of solely providing coded private information is not considered involvement. However, individuals who provide coded private information are considered involved if they collaborate on other activities related to the research, including (but not limited to) (1) study interpretation, or analysis of the data resulting from the coded information; or (2) authorship of presentations or manuscripts related to the research.

☐ *Obtaining identifiable private information or specimens includes but is not limited to: Using, studying, or analyzing for research purposes identifiable private information of specimens that have been provided to researchers from any source, and recorded in any fashion for research purposes and retained for any length of time, or that were already in the possession of the researcher.*

Note that the definition of "identifiable" is not the same as in the HIPAA regulations about health care records. Information that is considered an "identifier" by HIPAA regulations may not meet the federal

☐ A. The data are identifiable patient health information collected in Washington State that will be used for research purposes without the consent of the patient (whether living or deceased) or the patient's legally authorized representative.

Living: individuals who are alive according to applicable local and national regulations. With respect to specimens, data, and other information gathered without direct interaction with the individual: it is assumed that the individuals are living unless there is reason to think otherwise.

Washington State law: There is no Washington State law that defines "human subject". However, using identifiable patient health information collected in Washington State for research purposes, without the consent of the patient or the patient's legally authorized representative, requires IRB review (WA RCW 70.02.05). This applies to both living and deceased patients.

☐ B. The data are **about** individuals, and the individuals are **living**.

About: the data relates to the person. Asking individuals what they think about something (asking for an opinion) is almost always about the person. Asking for factual information, or other questions where the answers are expected to be independent of the person being asked, are generally not about the individual.

Examples:

- *A survey of elementary school teachers that asks them factual questions about class size, classroom features, and availability of classroom materials would generally not be considered to be **about** the teachers and would therefore not involve human subjects.*
- *A survey of elementary school teachers that asks them their **opinions** about the standard curriculum would generally be considered to be about the teachers.*
- *A researcher is developing a new user interface for a computer program. His research uses the "think aloud" method whereby he asks college students to verbally express their thought processes as they use the interface. Though the object of his interest is the interface, not the students, he is nonetheless collecting data **about** the students.*
- *Suppose you ask individuals, "How does your hospital respond to confidentiality breaches?" If you are seeking information about the hospital and are asking people who should know the answer, then the question is not about the person being asked. If you are seeking how often employees know the correct answer, then the question is about the person.*

Conclusion

If neither box is checked: human subjects are not involved, as defined by the Common Rule. Proceed to Part 6 to determine whether the activity is human subjects research as defined by the Food and Drug Administration (FDA).

If only box A is checked: proceed to Part 4.

If only box B is checked: proceed to Part 4.

If both boxes are checked: go to Part 4 to complete the determination about whether any federal human subjects regulations apply. However, regardless of outcome, the activity requires IRB review or exempt status because of Washington State law RCW 70.02.

END PART THREE

4. Human Subject as Defined by the Common Rule (45 CFR 46): Component 2

Check if "**YES**".

☐ The research is federally funded and involves the use of newborn dried bloodspots that are collected on or after March 18, 2015. Note that it does not matter whether the bloodspots are identifiable, coded, de-identified, or anonymous. *Per Newborn Screening Saves Lives Reauthorization Act of 2014.*

☐ The data are obtained through **intervention**.

Intervention: Physical procedures, or manipulations of the individuals or the individual's environment, that are performed for research purposes. Manipulations may be physical, social, psychological, or emotional. "Environment" includes an individual's social and virtual environments as well as physical environment.

*Obtain: Record in any fashion (writing, video, email, voice recording, etc.) for research purposes and retain for **any** length of time.*

Note: Individuals who "screen out" of a study because an intervention or interaction (such as a screening phone call or lab test) reveals that they do not meet the study eligibility criteria are still considered human subjects if they meet all of the criteria outlined in this Worksheet.

UNIVERSITY of WASHINGTON
HUMAN SUBJECTS DIVISION

WORKSHEET: Human Subjects Research

PURPOSE and INSTRUCTIONS

This worksheet provides support for individuals in determining whether an activity is human subjects research. It is completed and retained only when the activity is determined to be **Not Human Subjects Research**. The sections should be considered in the order presented. The term "data" refers to information of all types (information, records, specimens, recordings, photos, X-rays, etc.)

1. Are you a (select your position to reveal the correct Research Study Information box):

- ☒ Researcher or Research Coordinator, etc. (not HSD Staff)
- ○ HSD Staff Member

2. Research as defined by the Common Rule (45 CFR 46)

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

Check all that apply. These are the key concepts of the definition.

☐ A. **Systematic investigation**.
A detailed or careful examination that has or involves a prospectively identified approach to the activity based on a system, method, or plan.

☒ B. **Generalizable knowledge**.
The information is expected to expand the knowledge base of a scientific discipline or other scholarly field or study and yield one or both of the following:

- Results that are applicable to a larger population beyond the site of data collection or the specific subjects studied.
- Results that are intended to be used to develop, test, or support theories, principles, and statements of relationships, or to inform policy beyond the study.
- Case reports are usually considered to contribute to generalizable knowledge if they involve more than three cases.

☐ C. All of the following apply to the activity:

- ☐ The activity is designed to contribute to the solution of social and health problems, or the evaluation of public benefit and service programs.
- ☐ The activity involves the use of individually identifiable records from one or more of the following state institutions:
  - WA State Department of Social and Health Services (DSHS)
  - WA State Department of Corrections (DOC)
  - WA State Department of Health (DOH)
  - WA State Department of Early Learning
  - Any WA State Institution of higher education, including the UW and UW Medicine
- ☐ The records pertain only to living individuals.
- ☒ The records will be obtained and used without the informed consent of the person to whom the records pertain or the persons' legally authorized representatives.

Conclusion

All boxes are checked: the activity is Research as defined by the Common Rule. Proceed to Part 3.

If boxes A, and B are checked: the activity is Research as defined by the Common Rule. Proceed to Part 3.

All other combinations of checked boxes. The activity is not Research as defined by the Common Rule. Proceed to Part 6 to determine whether the activity is human subjects research as defined by the Food and Drug Administration (FDA).

END PART TWO

3. Human Subject as defined by the Common Rule (45 CFR 46): Component 1

Check all that apply.