SMG 9001.4

FDA STAFF MANUAL GUIDES, VOLUME IV – AGENCY PROGRAM DIRECTIVES

GENERAL OR MULTIDISCIPLINE

HUMAN SUBJECTS RESEARCH CONDUCTED OR SUPPORTED BY THE FDA

Effective Date: 02/19/2019

1. PURPOSE.

The purpose of this guide is to provide an overview of the Food and Drug Administration's (FDA's) policies and procedures for human subjects research conducted or supported by the FDA and the oversight of such research.[1]

2. POLICY.

The regulations at Code of Federal Regulations (CFR) Title 45, Part 46, Federal Policy for the Protection of Human Subjects (with Subpart A known as the "Common Rule"), describe requirements for research involving human subjects conducted, supported or otherwise subject to regulation by the U.S. Department of Health and Human Services, and accordingly for research involving human subjects conducted or supported by FDA.[2]

The FDA, including the FDA Institutional Review Board (IRB), will comply with 45 CFR Part 46 and FDA standard operating procedures (SOPs) regarding human subjects research conducted or supported by the FDA. In addition, such research and the FDA IRB must comply with FDA regulations (such as 21 CFR Part 50, 21

[1] This SMG replaces retired SMG 2111.3 (FDA Research Involving Human Subjects Research Committee (RIHSC)).

[2] This SMG is applicable to human subjects research conducted in compliance with the Pre-2018 Requirements or the 2018 Requirements under the Common Rule, as defined at 45 CFR 46.101(l)(1)-(2). The general compliance date for the 2018 Requirements is January 21, 2019; see the June 19, 2018 Final Rule for details (83 FR 28497).

CFR Part 56, 21 CFR Part 312, and/or 21 CFR Part 812), as applicable, and should generally follow applicable FDA and Office for Human Research Protections (OHRP) guidance documents.

All of FDA's human subjects research activities, regardless of whether the research is subject to regulation under the Common Rule or FDA regulations, will be guided by the ethical principles of respect for persons, beneficence, and justice, in accordance with The Belmont Report.

3. RESPONSIBILITIES.

To protect the rights, safety, and welfare, of human subjects in research conducted or supported by the FDA, the FDA is committed to:

- Conducting and providing oversight for human subjects research consistent with applicable laws, regulations, and policies;

- Ensuring FDA staff understand their responsibilities regarding human subjects research;

- Maintaining an IRB that functions consistent with 45 CFR Part 46 and 21 CFR Parts 50 and 56, and that exercises independent authority and decision making with respect to the review and approval of human subjects research; and

- Monitoring the progress of human subjects research funded by the FDA, where the FDA itself is not engaged[3] in the research.

The following sets out the roles and general responsibilities for FDA staff regarding human subjects research conducted or supported by the FDA and the review and/or oversight of such research.

A. Office of the Chief Scientist (OCS)

1. The Chief Scientist serves as the FDA's Institutional Official and is responsible for overseeing human subjects research conducted or supported by the FDA. On behalf of the FDA, the Chief Scientist assures protections for human subjects, including compliance with the Common Rule, as described in the FDA's Federalwide Assurance (FWA) for the Protection of Human Subjects on file with OHRP.[4] The Chief Scientist has the authority to approve requests for IRB authorization agreements (IAA) (see Section 5.A) and sign IAAs on behalf of FDA. In addition, research that has been approved by the

[3] See SOP on *Determining Whether FDA is Engaged in Nonexempt Human Subjects Research*; the FDA SOPs are posted in the central tracking system maintained by OCS.
[4] For a copy of the FDA's FWA, see the central tracking system.

FDA IRB may be subject to further appropriate review and approval or disapproval by the Chief Scientist (as well as other FDA officials) (see 45 CFR 46.112). However, the Chief Scientist and other FDA officials may not approve research if it has not been approved by an IRB (45 CFR 46.112).

2. The Human Subject Protection (HSP) Executive Officer in OCS provides centralized support, coordinates, and leads collaboration for human subject protection matters related to human subjects research conducted or supported by FDA. The HSP Executive Officer is responsible for activities including, but not limited to:

    - Verifying the initial determinations made by HSP Liaisons (see Section 3.B.2)

    - Supporting and assisting the Chief Scientist and the FDA IRB as related to human subjects research activities

    - Maintaining and proposing updates to applicable SOPs, based on established processes and timelines

3. The HSP Program Management Staff in OCS provides administrative support for human subjects research submissions to OCS and the FDA IRB, and for the FDA IRB activities. The HSP Program Management Staff is responsible for activities such as:

    - Managing all administrative aspects of the FDA IRB activities and preparing and maintaining IRB records

    - Verifying completeness of the FDA IRB submissions and other human subjects research submission packages to OCS

    - Performing data entry in the central tracking system, generating reports, and collecting metrics

B. FDA Centers[5]

1. Center or Office Directors[6] are accountable to the Commissioner (and the Chief Scientist who, on behalf of the FDA, assures protections for human subjects, including compliance with the Common Rule, as described in FDA's Federalwide Assurance for the Protection of Human Subjects) for human subjects research activities conducted or supported by their Center or Office. Center and Office Directors are responsible for activities such as:

[5] This SMG applies to all FDA.

[6] For purposes of this SMG, the term "Center or Office Directors" collectively refers to Center Directors, the Associate Commissioner for Regulatory Affairs, and Office Directors in the Office of the Commissioner.

- Designating HSP Liaisons (see Section 3.B.2)[7]
- Nominating FDA IRB Members and Alternate Members[8]
- Reviewing from their respective Center or Office:

    - Research studies submitted to the FDA IRB or that are the subject of other human subjects research submissions to OCS to verify scientific merit (or designating individuals from their Center or Office who will review such studies for scientific merit)

    - Submissions to the FDA IRB, and other human subjects research submissions to OCS, to ensure Center or Office concurrence with the contents of the research submission (for example, protocol, consent form, recruitment material, or determination form) (or designating individuals from their Center or Office who will review such submissions)

2. HSP Liaisons collaborate with the HSP Executive Officer and HSP Program Management Staff to facilitate oversight by OCS and/or IRB review for research conducted or supported by FDA, as appropriate. HSP Liaisons are accountable to their respective Center or Office Director. HSP Liaisons are responsible for activities such as:

    - Providing initial determinations as to whether:

        - An activity is research involving human subjects

        - Human subjects research is exempt under 45 CFR Part 46

        - The FDA's activity in nonexempt human subjects research constitutes FDA engagement

        - Nonexempt human subjects research meets the criteria for expedited IRB review

    - Assessing if the criteria for an IAA request are met

    - Confirming that review of research protocols for scientific merit by the Center Director (or designee) are completed prior to submission to the FDA IRB, as well as other human subjects research submissions to OCS

[7] OCS designates the HSP Liaison for the Office of the Commissioner.
[8] See SOP on *FDA IRB Members, Alternates, and Chair: Selection Process and Qualifications* for additional information.

- Reviewing the FDA IRB submissions, and other human subjects research submissions to OCS, for completeness

- Developing, in collaboration with the FDA Project Leads, as appropriate, an annual status report of Center research activities that were submitted to the HSP Executive Officer for a determination (see Sections 4.A-C for human subjects research, exempt research, and FDA engagement determinations) and that do not require an IRB review, and for providing the annual status report to the HSP Executive Officer

3. The FDA Project Lead[9] is the individual with primary responsibility for the FDA's involvement in a human subjects research project. An FDA Project Lead should be identified for each human subjects research project (regardless of whether the research is exempt from IRB review or whether there is an IAA). The FDA Project Leads are responsible for activities such as:

    - Preparing the study protocol, informed consent, and related documents, collaboratively with the Investigator(s) or the sponsor,[10] as appropriate to the FDA's role in the research

    - Collaborating with the HSP Liaison as needed (for example, to submit research to the FDA IRB for review or to make required reports)

    - Following applicable FDA SOPs and Center or Office procedures (for example, for preparing the FDA IRB submissions for initial and continuing review)

    - When the FDA has entered into an IAA to rely on IRB oversight provided by an external IRB (meaning that the FDA IRB will not review the research):

        - Following the terms of the IAA

        - Reporting proposed changes in the research, unanticipated problems involving risks to subjects or others (henceforth "unanticipated problems"), or serious or continuing noncompliance to the HSP Executive Officer (to inform the Chief Scientist) as required by FDA SOPs, in addition to making required reports to the reviewing IRB

[9] An FDA Project Lead may also be an FDA Investigator. When an individual fills multiple roles, the individual must comply with the requirements for all roles.
[10] Investigators are individuals involved in conducting human subjects research studies (see Section 3.B.5). Sponsors are individuals or other entities who initiate a clinical investigation, but do not actually conduct the investigation (see Section 3.B.4).

- Reporting to the HSP Executive Officer (to inform the Chief Scientist) decisions made by the reviewing IRB (for example, regarding initial approval and approval of proposed changes in a research activity, unanticipated problems, any serious or continuing noncompliance, and any suspension or termination of IRB approval), as required by FDA SOPs

- When the research is reviewed by the FDA IRB, ensuring that proposed changes in a research activity, unanticipated problems, any serious or continuing noncompliance, and any suspension or termination of IRB approval by another IRB reviewing the research are reported to the FDA IRB

- Maintaining accurate records of the FDA's involvement in the research

4. For FDA-regulated research, sponsors are individuals or other entities who initiate a clinical investigation but do not actually conduct the investigation.[11] For FDA-regulated human subjects research conducted or supported by FDA, the sponsor may or may not be the FDA. If the sponsor is the FDA, the FDA Project Lead will be the primary point of contact for OCS and the FDA IRB with respect to the research. Sponsors must comply with FDA regulations (for example, 21 CFR Parts 50, 54, 56, 312, and/or 812), 45 CFR Part 46, and 42 CFR Part 11, as applicable.

5. Investigators are individuals involved in conducting human subjects research studies.[12] For purposes of this SMG, when multiple individuals are involved in conducting research, the "Principal Investigator" (PI) has overall responsibility for the study and "associate investigators" participate with the PI. A human subjects research activity supported by FDA may or may not have an Investigator that is an FDA employee. FDA Investigators are responsible for activities such as the following, depending on the study activity they perform:

    - Collaborating with the FDA Project Lead to:

        - Facilitate IRB review, when required

[11] "Sponsor" is defined in FDA regulations at 21 CFR 50.3(e), 56.102(j), 312.3(b) and 812.3(n). An individual who both initiates and conducts a clinical investigation is referred to as a "sponsor-investigator." See 21 CFR 50.3(f), 56.102(k), 312.3(b), 812.3(o).

[12] Involvement in conducting human subjects research includes performing tasks such as: obtaining information about living individuals by intervening or interacting with them for research purposes; obtaining identifiable private information about living individuals for research purposes; obtaining the voluntary informed consent of individuals to be subjects in research; and studying, interpreting, or analyzing identifiable private information or data for research purposes.

- Report unanticipated problems and serious or continuing noncompliance

- Provide progress reports and final reports to the FDA IRB

- Conducting the study in accordance with the protocol and the terms of the IRB approval, and ensuring that any proposed changes have been reviewed and approved by the IRB before they are implemented, except when necessary to eliminate apparent immediate hazards to the subject

- Obtaining and documenting informed consent in accordance with 45 CFR Part 46 and, as applicable, 21 CFR Part 50

- Maintaining accurate records of study conduct

- Following FDA policy, including any applicable Center or Office policy and procedures regarding Investigator responsibilities

- Complying with 45 CFR Part 46, complying with any applicable FDA regulations (for example, 21 CFR Parts 50, 54, 56, 312, and/or 812), and adhering to the principles of good clinical practice

C. The FDA IRB

1. The FDA IRB exercises independent authority and decision-making with respect to the review and approval of human subjects research. The FDA IRB will have access to meeting space and sufficient staff to support the IRB's review and recordkeeping responsibilities. The FDA IRB may review and has authority to approve, require modifications in (to secure approval), or disapprove research conducted or supported by the FDA, in accordance with requirements at 45 CFR Part 46, and, as applicable, 21 CFR Parts 50 and 56.[13] Additional authorities of the FDA IRB associated with review and continuing oversight of such research are set forth in FDA SOPs. The FDA IRB reviews such research only after the applicable FDA Center/Office evaluates and confirms the scientific merit of the study. Responsibilities of the FDA IRB for research it reviews include:

   - Conducting initial and continuing review, reviewing proposed changes in a research activity, and reviewing reports of unanticipated problems and serious or continuing noncompliance

[13] The FDA IRB typically does not review human subjects research in which FDA is not engaged. See Section 5.B.

- Reporting to the Chief Scientist and to OHRP (in collaboration with the Chief Scientist) any unanticipated problems, any serious or continuing noncompliance, and any suspension or termination of IRB approval[14]

4. DETERMINING IF IRB REVIEW IS REQUIRED.

FDA policy is that all human subjects research conducted or supported by FDA must obtain FDA IRB approval or be covered by an approved IAA, unless the FDA Project Lead has obtained a determination from the HSP Executive Officer that the research is exempt or that FDA is not engaged in the research. The following outlines general procedures for FDA staff regarding human subjects research conducted or supported by the FDA and/or the oversight of such research. Staff must also refer to and follow all applicable FDA SOPs that provide more detailed instructions regarding the processes discussed below. It is important to note that if a research activity involves an FDA-regulated product, it may be an FDA-regulated clinical investigation for which IRB review is required under FDA regulations. Consult the FDA SOP on *Additional Considerations for FDA-Regulated Research* for activities that may be FDA-regulated clinical investigations.

A. Human Subjects Research Determination

It is important that FDA staff involved in research activities are aware of and understand what constitutes human subjects research under the Common Rule. (See Attachment A to this SMG for the definitions of "research" and "human subject" for purposes of 45 CFR Part 46.) Before an activity that might be human subjects research begins, the FDA staff member with primary responsibility for the project should evaluate whether the activity is "research" and, if so, whether that research involves "human subjects" based on the definitions of human subject and research under the Common Rule. FDA staff members may self-determine that the activity does not constitute human subjects research and thus, does not require IRB review or a determination from the HSP Executive Officer.[15] However, if FDA later determines that this self-determination was incorrect, the FDA staff member with primary responsibility for the research will be accountable for the incorrect determination and the FDA IRB and/or the Chief Scientist may take appropriate action to address related noncompliance.

If FDA staff have any questions or difficulties in determining whether an activity constitutes human subjects research, they should consult with their HSP Liaison or work with their HSP Liaison to request a determination from the HSP Executive Officer. FDA staff may also consult with their HSP Liaison or work with their HSP Liaison to request a human subjects research determination from the HSP Executive Officer even if they believe that determination is straightforward.

[14] See SOP on *Unanticipated Problems Involving Risks to Subjects or Others, Serious or Continuing Noncompliance, and Suspension of Termination of IRB Approval*.

[15] FDA staff should follow any additional procedures or processes that their Centers/Offices may develop related to making a self-determination that the activity does not constitute human subjects research.

When requesting a determination from the HSP Executive Officer, the HSP Liaison should provide a recommendation. If the HSP Liaison recommends that the activity does not meet the definition of human subjects research, the HSP Liaison, in collaboration with the FDA staff member with primary responsibility for the activity, completes and enters the human subjects research determination form with supporting information in the central tracking system to request confirmation of that determination from the HSP Executive Officer. The HSP Executive Officer may consult the FDA IRB Chair and the Office of the Chief Counsel (OCC) as needed in determining whether the activity constitutes human subjects research.

If changes are proposed to an ongoing activity that could affect the previous human subjects research determination, the FDA staff member with primary responsibility for the activity should follow the process described above regarding evaluating whether proposed changes impact the previous determination related to whether the activity is human subjects research. If a determination from the HSP Executive Office is desired regarding the proposed changes, the FDA staff member with primary responsibility for the activity, in collaboration with the HSP Liaison, must complete a human subjects research determination form with supporting information in the central tracking system to request confirmation of that determination from the HSP Executive Officer, as described in the paragraph above.

An activity or proposed changes to an activity may not be implemented until the human subjects research determination is completed. If a determination is made that the activity meets the definition of human subjects research, either as an initial determination or in response to proposed changes to the activity, an evaluation should be made to determine whether the research is exempt (see Sections 4.B, below). If the activity does not meet the definition of human subjects research, either as an initial determination or regarding proposed changes, the activity may proceed without review and approval by the FDA IRB unless IRB review is required under FDA regulations.[16] A determination that an activity does not constitute human subjects research does not relieve the FDA staff involved in the activity from any responsibilities and requirements under other applicable laws or policies. For an activity that does not constitute human subjects research, the applicable FDA Center/Office is responsible for oversight of that activity.

B. Exempt Research Determination

Certain categories of human subjects research are considered exempt under 45 CFR Part 46. The HSP Liaison, in collaboration with the FDA Project Lead, conducts an initial evaluation of whether the research is exempt. If the HSP Liaison makes an initial determination that the research is nonexempt, the HSP

[16] Consult the SOP on *Additional Considerations for FDA-Regulated Research* for activities that may be FDA-regulated clinical investigations.

Liaison should proceed to evaluating whether FDA is engaged in the research (see Section 4.C, below). If the HSP Liaison makes an initial determination that the research is exempt, the HSP Liaison, in collaboration with the FDA Project Lead, completes and enters the exempt research determination form with supporting information in the central tracking system to request confirmation of that determination from the HSP Executive Officer. The HSP Executive Officer may consult the FDA IRB Chair and OCC as needed in determining whether the research is exempt.

If the activity is human subjects research that is exempt under 45 CFR Part 46, the activity may proceed without review and approval by the FDA IRB, unless the exemption category requires limited IRB review under the 2018 Common Rule requirements or IRB review is required under FDA regulations.[17]

If changes are proposed to ongoing human subjects research that could affect its exempt status, the HSP Liaison, in collaboration with the FDA Project Lead, must complete a new exemption determination form with supporting information in the central tracking system to request confirmation of that determination from the HSP Executive Officer, as described in the paragraph above. The proposed change may not be implemented before receiving confirmation of exemption from the HSP Executive Officer, except when the proposed changes are necessary to eliminate apparent immediate hazards to the subject. If the research, with the proposed change, continues to qualify as exempt, the activity may proceed without review and approval by the FDA IRB, unless the exemption category requires limited IRB review under the 2018 Common Rule requirements or IRB review is required under FDA regulations.

A determination that the human subjects research is exempt does not relieve the FDA staff involved in the activity from any responsibilities or requirements under other applicable laws or policies. For an activity that falls under an exempt category, the applicable FDA Center/Office is responsible for oversight of that activity.

C. FDA Engagement Determination

If the HSP Liaison makes an initial determination that the activity is nonexempt human subjects research, the HSP Liaison, in collaboration with the FDA Project Lead, evaluates whether the FDA's role in the activity constitutes engagement in the research.[18] If the HSP Liaison makes an initial determination that the FDA is engaged in human subjects research, the HSP Liaison and FDA Project Lead will follow the applicable procedures under Section 5.A, below. If the HSP Liaison makes an initial determination that the FDA is not engaged in human subjects research, the HSP Liaison, in collaboration with the FDA Project Lead, completes and enters the FDA engagement determination form with supporting information

[17] See SOP on *Determining Whether Human Subjects Research is Exempt*.
[18] See SOP on *Determining Whether FDA is Engaged in Nonexempt Human Subjects Research*

in the central tracking system to request confirmation of that determination from the HSP Executive Officer. The HSP Executive Officer may consult the FDA IRB Chair and OCC as needed in determining whether FDA is engaged in human subjects research.

If changes are proposed to ongoing human subjects research that could make FDA engaged in the research, the HSP Liaison, in collaboration with the FDA Project Lead, must complete a new engagement determination form with supporting information in the central tracking system to request confirmation of that determination from the HSP Executive Officer, as described in the paragraph above. The proposed change may not be implemented before receiving confirmation of the new engagement determination from the HSP Executive Officer except when the proposed changes are necessary to eliminate apparent immediate hazards to the subject.

A determination that FDA is not engaged in nonexempt human subjects research does not relieve the FDA staff involved in the activity from any responsibilities and requirements under other applicable laws or policies. For human subjects research in which FDA is not engaged, the applicable FDA Center/Office is responsible for oversight of FDA activities related to that research.[19]

5. IRB OVERSIGHT OF NONEXEMPT HUMAN SUBJECTS RESEARCH CONDUCTED OR SUPPORTED BY THE FDA

IRB oversight is required for human subjects research conducted or supported by the FDA that is not exempt from 45 CFR Part 46 or for which such oversight is required by FDA regulations.

A. When the FDA is engaged in nonexempt human subjects research (see Section 4.C on FDA Engagement Determination), one of the following is required:

- Review and Approval by the FDA IRB – The FDA Project Lead (in collaboration with the Investigator(s) and HSP Liaison), before initiating the research, must seek review and obtain approval from the FDA IRB in accordance with the FDA IRB procedures;[20] or

- An IRB Authorization Agreement (IAA) – IAAs are written agreements through which an institution relies on an external IRB to provide IRB oversight of the research (for example, the FDA may rely on an IRB external to the FDA to review nonexempt human subjects research conducted or supported by the FDA).

    - IAA requests are reviewed for an approval decision by the Chief Scientist.

[19] When FDA is not engaged in the research, also see Section 5.B.
[20] Refer to SOP on *FDA Institutional Review Board (IRB) Submissions*.

- Regardless of whether the IRB of record is the FDA IRB or an external IRB, the FDA retains certain responsibilities under 45 CFR Part 46.

- The HSP Liaison (in collaboration with the FDA Project Lead and the Investigator(s)), determines if the nonexempt human subjects research meets the criteria to request an IAA.[21] The HSP Liaison completes and enters the IAA request with supporting information in the central tracking system. The HSP Executive Officer works with the FDA IRB Chair to provide an evaluation of the IAA request to the Chief Scientist. OCC may be consulted as needed. Notification of the approval decision for the IAA request should generally be provided to the HSP Liaison by the HSP Executive Officer within 15 business days of submission in the central tracking system.

B. When the FDA provides funding or other support for nonexempt human subjects research and is not engaged in that research for purposes of 45 CFR Part 46 (see Section 4.C on FDA Engagement Determination), the institutions that are engaged are responsible for protecting the rights, safety, and welfare of human subjects involved in the research. Unless the funding instrument (for example, a grant) or other agreement specifies differently, or IRB review is required under FDA regulations, review by the FDA IRB or an IAA is not required. Such research funded or supported by the FDA remains subject to the requirements in 45 CFR Part 46.

6. REFERENCES.

A. Regulations

45 CFR Part 46 Federal Policy for the Protection of Human Subjects
21 CFR Part 50 Protection of Human Subjects
21 CFR Part 54 Financial Disclosure by Clinical Investigators
21 CFR Part 56 Institutional Review Boards
21 CFR Part 312 Investigational New Drug Application
21 CFR Part 812 Investigational Device Exemptions
42 CFR Part 11 Clinical Trials Registration and Results Information Submission

B. Additional Resources

- The Belmont Report
- FWA for the FDA
- Definitions (Attachment A)

[21] Refer to SOP on *Institutional Review Board Authorization Agreements When FDA is the Relying Institution: Criteria and Submission Process*.

7. EFFECTIVE DATE.

The effective date of this guide is February 19, 2019.

8. Document History -- SMG 9001.4, Human Subjects Research Conducted or Supported by the FDA

STATUS (I, R, C)	DATE APPROVED	LOCATION OF CHANGE HISTORY	CONTACT	APPROVING OFFICIAL
Initial	01/30/2019	N/a	OC/OCS	RADM Denise Hinton, Chief Scientist, OCS

Back to General Administration, Volume III (2000-3999)

Attachment A – Definitions, for the purposes of this SMG

Human Subject (2018 Common Rule) – A living individual about whom an investigator (whether professional or student) 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 (45 CFR 46.102(e)(1)).

Human Subject (pre-2018 Common Rule) – A living individual about whom an investigator (whether professional or student) conducting research obtains: data through intervention or interaction with the individual or identifiable private information (45 CFR 46.102(f)).

Institutional Authorization Agreement (IAA) – An agreement between institutions to designate IRB responsibilities and document the relying and reviewing institutions.

Intervention (2018 Common Rule) – Includes both physical procedures by which information or biospecimens are gathered (e.g., venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes (45 CFR 46.102(e)(2)).

Intervention (pre-2018 Common Rule) – Includes both physical procedures by which data are gathered (for example, venipuncture) and manipulations of the subject or the subject's environment that are performed for research purposes. **Interaction** includes communication or interpersonal contact between investigator and subject. **Private information** includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and 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). Private information must be individually identifiable (i.e., 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 research involving human subjects (45 CFR 46.102(f)).

Interaction (2018 Common Rule) – Includes communication or interpersonal contact between investigator and subject (45 CFR 46.102(e)(3)).

Private information (2018 Common Rule) - Includes information about behavior that occurs in a context in which an individual can reasonably expect that no observation or recording is taking place, and information that has been provided for specific purposes

by an individual and that the individual can reasonably expect will not be made public (e.g., a medical record) (45 CFR 46.102(e)(4)).

Identifiable private information (2018 Common Rule) – Private information for which the identity of the subject is or may readily be ascertained by the investigator or associated with the information (45 CFR 46.102(e)(5)).

Identifiable biospecimen (2018 Common Rule) – A biospecimen for which the identity of the subject is or may readily be ascertained by the investigator or associated with the biospecimen (45 CFR 46.102(e)(6)).

Research (2018 Common Rule) – A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program that is considered research for other purposes. For example, some demonstration and service programs may include research activities. For purposes of the 2018 Common Rule, the following activities are deemed not to be research:

(1) Scholarly and journalistic activities (e.g., oral history, journalism, biography, literary criticism, legal research, and historical scholarship), including the collection and use of information, that focus directly on the specific individuals about whom the information is collected.

(2) Public health surveillance activities, including the collection and testing of information or biospecimens, conducted, supported, requested, ordered, required, or authorized by a public health authority. Such activities are limited to those necessary to allow a public health authority to identify, monitor, assess, or investigate potential public health signals, onsets of disease outbreaks, or conditions of public health importance (including trends, signals, risk factors, patterns in diseases, or increases in injuries from using consumer products). Such activities include those associated with providing timely situational awareness and priority setting during the course of an event or crisis that threatens public health (including natural or man-made disasters).

(3) Collection and analysis of information, biospecimens, or records by or for a criminal justice agency for activities authorized by law or court order solely for criminal justice or criminal investigative purposes.

(4) Authorized operational activities (as determined by each agency) in support of intelligence, homeland security, defense, or other national security missions (45 CFR 46.102(l)).

Research (pre-2018 Common Rule) – A systematic investigation, including research development, testing, and evaluation, designed to develop or contribute to generalizable knowledge. Activities that meet this definition constitute research for purposes of this policy, whether or not they are conducted or supported under a program which is considered research for other purposes. For example, some demonstration and service programs may include research activities (45 CFR 46.102(d))