Title: The Revised Federal Policy for the Protection of Human Subjects - A Summary, and an Implementation Roadmap and Matrix
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THE REVISED FEDERAL POLICY FOR THE PROTECTION OF HUMAN SUBJECTS

A Summary, and an Implementation Roadmap and Matrix

Background

On January 19, 2017, the U.S. Department of Health and Human Services (HHS) and fifteen other Federal Departments and Agencies announced revisions to modernize, strengthen, and make more effective the Federal Policy for the Protection of Human Subjects that was originally promulgated as a *Common Rule* in 1991. The Final Rule will be effective January 21, 2019, with the exception of *cooperative research* (single IRB review) which will not be effective until January 20, 2020. The key revised elements of the federal policy are outlined in the table below:

Additional References
- *NEJM 2017*
- *Health Affairs 2017*

Table 1

KEY REVISED SECTIONS	IMPACT TO RESEARCH	ADDITIONAL GUIDANCE
APPLICABILITY		
▪ 45 CFR 46.101(a)	** 45 CFR 46 APPLIES TO FEDERALLY-SUPPORTED RESEARCH ** Exempt Category Research is exempt from the 45 CFR 46 requirements	** DOJ, FDA, AND CPSC HAS YET TO ADOPT THE REVISED 45 CFR 46 ** Preamble (page 113) SACHRP (compliance dates/transition provisions), May 2017 - Attachment A
▪ 45 CFR 46.101(f)	When applicable, American Indian and Alaska Native Tribal Laws will be applied	Preamble (page 155)
DEFINITIONS		
▪ 45 CFR 46.102(e)	The definition of *Human Subjects* includes *identifiable biospecimens*	Preamble (page 268)
▪ 45 CFR 46.102(l)	Provides examples of what are not considered *human subjects research*: - Scholarly/Journalistic activities - Public Health Surveillance - Collection/Analysis of information/biospecimens/records for/by a criminal justice agency - Authorized operational activities by an agency for intelligence, homeland security, defense, or national security missions	Preamble (page 324)
▪ 45 CFR 46.102(m)	Defines *Written (or, in writing)* as paper or electronic format	Preamble (page 426)

EXEMPT CATEGORY RESEARCH		
▪ 45 CFR 46.104(b)	Subpart B (Pregnant Women, Human Fetuses, and Neonates) is applicable if the conditions of the exemptions are met Subpart C (Prisoners) is not applicable except for research aimed at involving a broader subject population that only incidentally includes prisoners Subpart D (Children) is applicable to categories 1 and 4, 5, 6, 7, and 8 if the conditions of the exemption are met Subpart D is applicable to category 2(i and ii) when the investigator(s) do not participate in the activities being observed; category 2(iii) is not applicable	Preamble (page 458) 2017 AJB
▪ 45 CFR 46.104(d)	Exempt categories 1-2 and 5 are further defined, and 6 remains the same - 1: normal educational practices not likely to adversely impact students' opportunity to learn - 2: criteria iii specifies that an IRB can conduct a limited review for studies in which identifiable information is obtained/recorded - 5: new section for research conducted by Federal employees New categories are 3-4, and 7-8 - 3: research involving benign behavioral interventions with adult subjects, in conjunction with the collection (verbal, written, data entry, audio/visual recording) of information is permitted with prospective consent and at least one of three additional criteria are met - 4: secondary research for which consent is not required is permitted if at least one of three additional criteria are met - 7: store/maintain identifiable private information/specimens for potential secondary research permitted by a limited IRB review - 8: research involving the use of identifiable private information/specimen for secondary research use for which broad consent is required, is permitted when 3 additional criteria are met	Preamble (page 493) SACHRP, July 2017 - Attachment B SACHRP (HIPAA Exemption), October 2017 - Attachment B Figures 1, 2, and 3 (pages 6-7, below)
IRB REVIEW OF RESEARCH		
▪ 45 CFR 46.109(a)	Describes Exempt Research that require limited IRB review as a condition of exemption **Limited IRB Review* is performed at an IRB Expedited Subcommittee meeting by an IRB Chair or an IRB Chair-designee	Preamble (page 749) OHRP, July 2018 - Removes requirement of IRB's review of the grant
▪ 45 CFR 46.109(f)	Describes when continuing review is not required: - Research eligible for expedited review - Research reviewed by the Limited IRB review Process - Research limited to only: data analysis, or accessing follow-up clinical data (performed as part of clinical care)	Preamble (page 750) FDA, October 2018 - Guidance

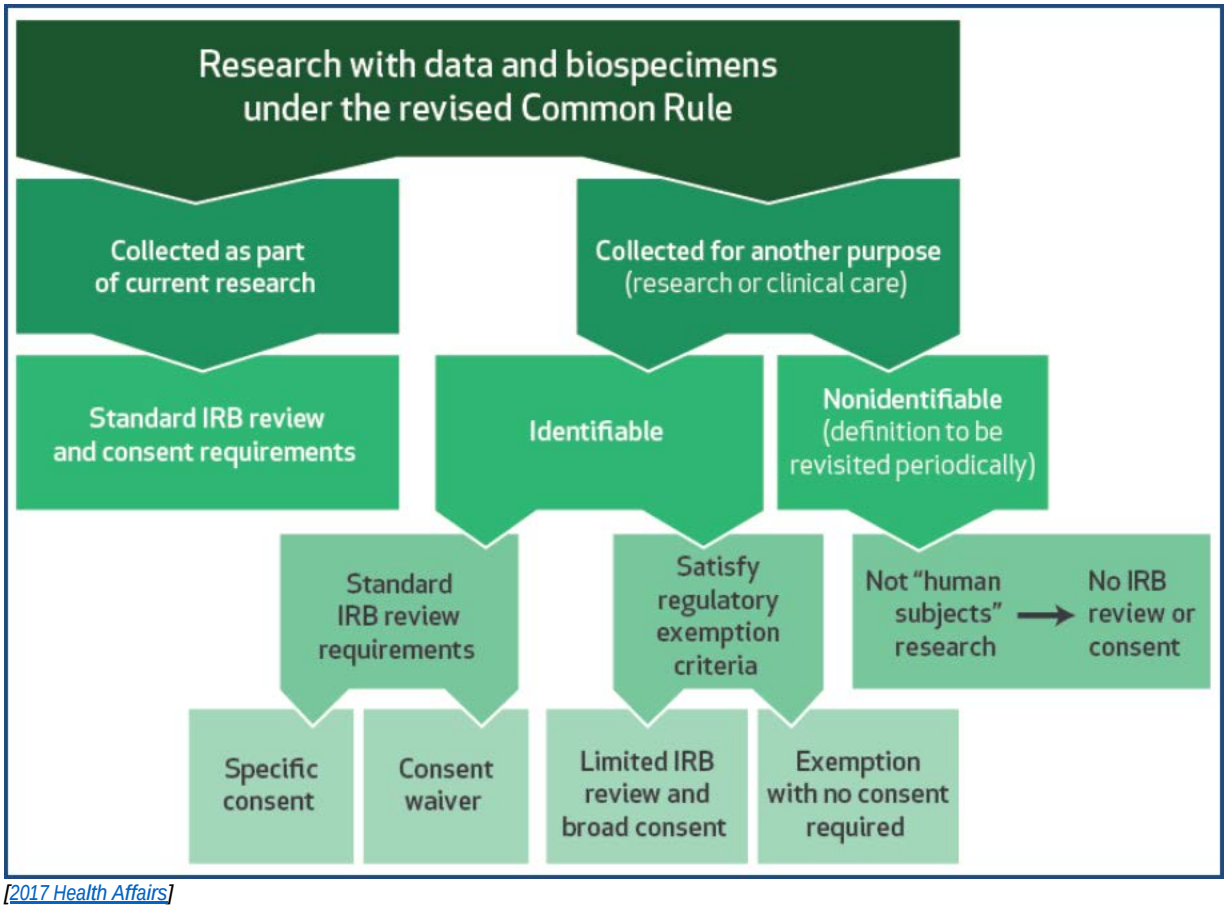
EXPEDITED REVIEW PROCEDURE		
▪ 45 CFR 46.110(a)	List of categories will be evaluated every 8 years	Preamble (page 761) SACHRP, October 2017 - Attachment A SACHRP, March 2018 - Attachment A SACHRP, July 2018 - Attachment F, not yet available FDA, October 2018 - Guidance
▪ 46.110(b)(1)	Parameters for Expedited Review includes a third criteria: - Research for which limited IRB review is a condition of exemption [Exempt categories 2(iii), 3(i), 7-8]	Preamble (page 761)
CRITERIA FOR IRB APPROVAL		
▪ 45 CFR 46.111(a)(3) and 45 CFR 46.111(b)	Removes *pregnant women* and *handicapped/mentally disabled* as a vulnerable population Specifies individuals with *impaired decision-making capacity* and *economically/educationally disadvantaged* as a vulnerable population	Preamble (page 772) NIH IAL Policy, 2019
▪ 45 CFR 46.111(a)(7)(i)	Include adequate provisions to protect privacy of subjects / maintain confidentiality of data - HHS guidance is forthcoming	Preamble (page 776) SACHRP, March 2018 (EU GDPR) - Attachment B - Addendum SACHRP, July 2018 (EU GDPR and Consent) - Attachment G, not yet available
▪ 45 CFR 46.111(a)(8)	Approval criteria for a limited IRB Review: - Broad consent for storage, maintenance, and secondary research use of identifiable information/specimens is obtained through informed consent [46.116(a)(1)-(4), and (a)(6), and 46.116(d)] - Broad consent (or waiver) is obtained [46.117) - If there is a change in the way identifiable private information/specimens are stored/maintained, there are provisions to protect the privacy of subjects and maintain confidentiality of data	Preamble (page 783)
COOPERATIVE RESEARCH		
▪ 45 CFR 46.114(b), and 45 CFR 46.114(c)	Any institution engaged in cooperative research must rely upon approval by a single IRB for that portion of the research that is conducted in the US ▪ Exceptions: - Cooperative research for which more than single IRB review is required (i.e., American Indian or Alaska Native tribal law) - Research for which any federal department/agency supporting/conducting the research determines/documents that the use of a single IRB is not appropriate for the particular context For research not subject to 46.114(b), an institution participating in a cooperate project may enter into a joint review arrangement (or rely upon the review of another IRB, or make similar arrangements) to avoid duplication of effort	Preamble (page 799) NIH, 10/11/17 - Exceptions - Exceptions Process UCOP, 11/13/17 - NIH sIRB Policy - sIRB Reliance SACHRP, March 2018 - Attachment D NIH, 9/12/18 - Multi-Site Research Resource and Infrastructure Development

IRB RECORDS		
▪ 45 CFR 46.115(a)(3)	Include a rationale for conducting continuing review of research that otherwise would not require continuing review [46.109(f)(1)]	Preamble (page 814) FDA, October 2018 - Guidance
▪ 45 CFR 46.115(a)(8)	Include a rationale for an expedited reviewer's determination [46.110(b)(1)(i)] that research appearing on the expedited review list [46.110(a)] is more than minimal risk	Preamble (page 814)
INFORMED CONSENT		
▪ 45 CFR 46.116(a) and (b) ▪ 45 CFR 46.116(a)(4)	Specifies *representative* as the *legally authorized representative* Specifies that the subject/LAR must be provided with the information that a reasonable person would want to have in order to make an informed decision, and an opportunity to discuss that information	Preamble (page 840) California Newborn Blood Spot regulation 2017 Hastings Center Report FDA, October 2018 - Guidance HHS, 9/7/18 - Informed Consent standards NAS, 7/10/18 - Returning Individual Research Results NIH, 2015 - GDS Policy NIH, 2015 - Update to Data Management of Genomic Summary Results Under the NIH GDS Policy NIH, 5/30/17 - Recommendations for Returning Research Results NIH, 11/1/18, Management of Genomic Summary Results Access - NOT-OD-19-023 SACHRP, May 2017 - Appendix F SACHRP, July 2017 - Attachment C - Attachment D SACHRP, March 2018 - Attachment A - Attachment C SACHRP, July 2018 - Attachment A, not yet available
▪ 45 CFR 46.116(a)(5)	Begin with a concise and focused presentation of the key information, and organized/presented in a format that facilitates comprehension Present information in sufficient detail relating to the research, and organized/presented in a format that facilitates the subjects'/LARs' understanding for or against participation	
▪ 45 CFR 46.116(b)(9)	When this scenario is possible, include a statement that identifiers might be removed, and after such removal, the information/specimen could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject/LAR; or	

	Include a statement that the subject's information/specimen collected as part of the research, even when identifiers are removed, will not be used or distributed for future research	
▪ 45 CFR 46.116(c)(7)	Include a statement that the subject's specimens (even when identifiers are removed) may be used for commercial profit and whether the subject will/will not share in the commercial profit	
▪ 45 CFR 46.116(c)(8)	Include a statement whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions	
▪ 45 CFR 46.116(c)(9)	Include a statement whether the research will (if known) or might include whole genome sequencing	
▪ 45 CFR 46.116(d)	Describes the 7 elements of a broad consent form	
▪ 45 CFR 46.116(e)	Describes the elements for a waiver, and the elements for an alteration, of consent that involves public benefit/service programs conducted by/subject to the approval of state/local officials IRB must determine and document that the research meets 46.116(e)(3)(i) and (ii)	Preamble (page 936)
▪ 45 CFR 46.116(f)	Describes the *general* waiver or alteration of consent Waiver: - waiver of ICF permitted if 46.116(f)(3) has been met - if a subject was asked to provide broad consent for storage/maintenance/secondary research use of identifiable private information/specimen [46.116(d)], and refused to consent, an IRB cannot waive consent for the storage/maintenance/secondary research use of the identifiable private information/specimen Alteration: - IRB may approve a consent procedure that omits some, or alters some or all, of the elements of the informed consent provided that the IRB satisfies the requirements of 46.116(f)(3) - IRB may not omit or alter any of the requirements in 46.116(a) - If a broad consent is used, an IRB may not omit or alter any of the elements required in 46.116(d) IRB must determine and document the research meets 46.116(f)(3) and the additional new elements (ii, iii, v)	Preamble (page 959)
▪ 45 CFR 46.116(g)	Screening, recruiting, determining eligibility is permitted when: - LR will obtain information through oral or written communication with the prospective subject/LAR, or - LR will obtain identifiable private information/specimen by accessing records/stored identifiable specimens	Preamble (page 969)
▪ 45 CFR 46.116(h)	When a clinical trial has reached the status of *close to recruitment*, posting one IRB-approved clinical trial consent form is required for a clinical trial conducted/supported by a federal department/agency, and must be posted by the awardee or the federal department/agency at a publicly available federal website If the federal department/agency supporting/conducting the clinical trial determines that certain information (i.e., confidential commercial information) should not be made publicly available on a federal website, the federal department/agency may permit or require redactions to the information posted	Preamble (page 981) HHS, 8/28/18 Post to: - ClinicalTrials.gov, or - a docket folder on Regulations.gov (Docket ID: HHS-OPHS-2018-0021)
▪ 45 CFR 46.116(i) and 45 CFR 46.116(j)	The Informed Consent requirements does not preempt other applicable federal, state, or local laws, including American Indian or Alaska Native tribal laws that require additional information to be disclosed	Preamble (page 1286)

	45 CFR 46 does not limit the authority of a physician to provide emergency medical care, to the extent the physician is permitted to do so under applicable Federal, state, or local law (including tribal law passed by the official governing body of an American Indian or Alaska Native tribe)	
DOCUMENTATION OF INFORMED CONSENT		
▪ 45 CFR 46.117(a)	Includes electronic format	
▪ 45 CFR 46.117(b)(2)	Ensure that the key information [46.116(a)(5)(i)] was presented first to the subject	Preamble (page 1005) FDA, October 2018 - Guidance
▪ 45 CFR 46.117(c)(1)(iii)	A waiver of documentation of informed consent includes a new third criteria: - if the subject/LAR are members of a distinct cultural group/community in which signing forms is not the norm, an IRB may waive requirement of documentation of informed consent when the research presents no more than minimal risk of harm to subjects and provided there is an appropriate alternative mechanism for documenting that informed consent was obtained	Preamble (page 1006)
▪ 45 CFR 46.117(c)(2)	When documentation of informed consent is waived, the IRB may require (subjects and) LARs to receive a written statement regarding the research	

Figure 1: Data, Biospecimens, Consent, and IRB Review



[2017 Health Affairs]

Figure 2: Determination of Non-Exempt Human Subjects Research

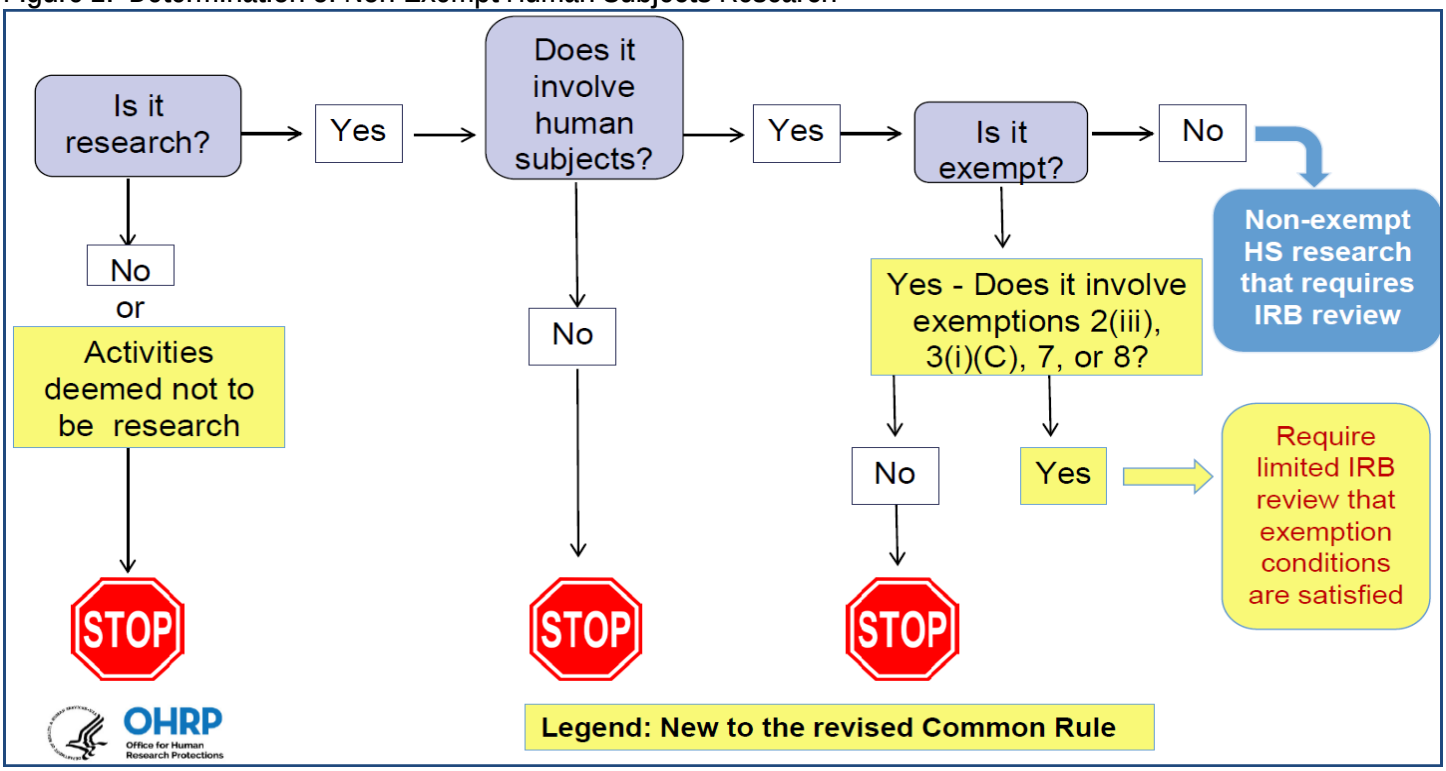


Figure 3: Secondary Research