COMPARISON OF HHS COMMON RULE 45 CFR 46
(BOTH PRE-2018 AND 2018 REQUIREMENTS)
AND FDA REGULATIONS 21 CFR 50 (*et seq*.)

Contents

Introduction

This tool is a regulatory comparison of informed consent regulations, comparing the pre-2018 HHS Common Rule (45 CFR 46) to the 2018 HHS Common Rule, FDA and 61 FR 51531. The use of broad consent for the storage, maintenance and secondary research use of identifiable private information or identifiable biospecimens, as described in the 2018 Common Rule at 45 CFR 46.116(d) is not implemented by the NIH at this time. There is OHRP and FDA guidance on consent that should also be considered. We provide links to these guidance in **Additional References**.

Notes:

- In the tables below when there are similar clauses but the language differs, we have bolded the text for the reader to highlight the regulatory differences.
- Italicized language either mirrors italicization in the regulation, or provides information about the regulation.

General Elements of Informed Consent			
Topic	**Pre-2018 Common Rule 45 CFR 46.116**	**2018 Common Rule 45 CFR 46.116(a)**	**FDA Regulations 21 CFR 50.23**
General	*No comparable provision in the Pre-2018 Common Rule*	**(a)** *General.* General requirements for informed consent, whether written or oral, are set forth in this paragraph and apply to consent obtained in accordance with the requirements set forth in paragraphs (b) through (d) of this section.	*No comparable provision in 21 CFR Part 50*
General - Broad Consent;	*No comparable provision in the Pre-2018 Common Rule*	Broad consent may be obtained in lieu of informed consent obtained in accordance with paragraphs (b) and (c) of this section only with respect to the storage, maintenance, and secondary research uses of identifiable private information and identifiable biospecimens.	*No comparable provision in 21 CFR Part 50*
Legally Effective Informed Consent Required before involving a human being in research	Except as provided elsewhere in this policy, no investigator may involve a human being as a subject in research covered by this policy unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.	Except as provided elsewhere in this policy**:** **(1)** Before **involving** a human subject in research covered by this policy, **an** investigator **shall** obtain the legally effective informed consent of the subject or the subject's legally authorized representative.	Except as provided **in §50.23 and §50.24**, no investigator may involve a human being as a subject in research covered by **these regulations** unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.

General Elements of Informed Consent			
Topic	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116(a)**	**FDA Regulations** **21 CFR 50.23**
Sufficient opportunity to consider participation	An investigator shall seek such consent only under circumstances that provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate and that minimize the possibility of coercion or undue influence.	**(2)** An investigator shall seek informed consent only under circumstances that provide the prospective subject or the **legally authorized** representative sufficient opportunity to discuss and consider whether or not to participate and that minimize the possibility of coercion or undue influence.	*Same clause as in the Pre-2018 Common Rule.*
Language understandable to subject	The information that is given to the subject or the representative shall be in language understandable to the subject or the representative.	**(3)** The information that is given to the subject or the **legally authorized** representative shall be in language understandable to the subject or the legally authorized representative.	*Same clause as in the Pre-2018 Common Rule.*
Information required to make a decision	*No comparable provision in the Pre-2018 Common Rule*	**(4)** The prospective subject or the legally authorized representative must be provided with the information that a reasonable person would want to have in order to make an informed decision about whether to participate, and an opportunity to discuss that information.	*No comparable provision in 21 CFR Part 50*
Key information	*No comparable provision in the Pre-2018 Common Rule*	**(5)** Except for broad consent obtained in accordance with paragraph (d) of this section: **(i)** Informed consent must begin with a concise and focused presentation of the key information that is most likely to assist a prospective subject or legally authorized representative in understanding the reasons why one might or might not want to participate in the research. This part of the informed consent must be organized and presented in a way that facilitates comprehension.	*No comparable provision in 21 CFR Part 50*

General Elements of Informed Consent			
Topic	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116(a)**	**FDA Regulations** **21 CFR 50.23**
Facilitates understanding	*No comparable provision in the Pre-2018 Common Rule*	**(ii)** Informed consent as a whole must present information in sufficient detail relating to the research, and must be organized and presented in a way that does not merely provide lists of isolated facts, but rather facilitates the prospective subject's or legally authorized representative's understanding of the reasons why one might or might not want to participate.	*No comparable provision in 21 CFR Part 50*
Exculpatory Language	No informed consent, **whether oral or written,** may include any exculpatory language through which the subject or the representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution or its agents from liability for negligence.	**(6)** No informed consent may include any exculpatory language through which the subject or the **legally authorized** representative is made to waive or appear to waive any of the subject's legal rights, or releases or appears to release the investigator, the sponsor, the institution, or its agents from liability for negligence.	*Same as the clause in the Pre-2018 Common Rule.*

Basic Elements of Informed Consent			
TOPIC	**Pre-2018 Common Rule 45 CFR 46.116**	**2018 Common Rule 45 CFR 46.116(b)**	**FDA Regulations 21 CFR 50.25**
General	**(a)** *Basic elements of informed consent.* Except as provided in paragraph (c) or (d) of this section, in seeking informed consent the following information shall be provided to each subject:	**(b)** *Basic elements of informed consent.* Except as provided in paragraph **(d), (e),** or **(f)** of this section, in seeking informed consent the following information shall be provided to each subject **or the legally authorized representative**:	**(a)** *Basic elements of informed consent.* In seeking informed consent, the following information shall be provided to each subject:
Explanation of research	**(1)** A statement that the study involves research, an explanation of the purposes of the research and the expected duration of the subject's participation, a description of the procedures to be followed, and identification of any procedures which are experimental;	*NOTE: Section (b) of the 2018 Common Rule at 46.116, clauses (b) (1) through (b)(5) are identical to Section (a)(1) through (a)(5) of the Pre-2018 Common Rule at 46.116 (See second column to the left) and therefore have been omitted here.*	*NOTE: Section (a) of the FDA Regulations at 21 CFR 50.25, clauses (a) (1) through (a)(4) are identical to clauses (a)(1) through (a)(4) of the Pre-2018 Common Rule at 46.116 (See second column to the left) and therefore have been omitted here.*
Foreseeable risks	**(2)** A description of any reasonably foreseeable risks or discomforts to the subject;		
Benefits	**(3)** A description of any benefits to the subject or to others which may reasonably be expected from the research;		
Alternatives	**(4)** A disclosure of appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the subject;		
Confidentiality	**(5)** A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained;		**(5)** A statement describing the extent, if any, to which confidentiality of records identifying the subject will be maintained **and that notes the possibility that the Food and Drug Administration may inspect the records.**

Basic Elements of Informed Consent			
TOPIC	**Pre-2018 Common Rule 45 CFR 46.116**	**2018 Common Rule 45 CFR 46.116(b)**	**FDA Regulations 21 CFR 50.25**
More than Minimal Risk	**(6)** For research involving more than minimal risk, an explanation as to whether any compensation and an explanation as to whether any medical treatments are available if injury occurs and, if so, what they consist of, or where further information may be obtained;	*NOTE: Section (b) of the 2018 Common Rule at 46.116, clauses (b)(6) through (b)(8) are identical to clauses (a)(6) through (a)(8) of the Pre-2018 Common Rule at 46.116 (See second column to the left) and therefore have been omitted here.*	*NOTE: Section (a) of the FDA Regulations at 21 CFR 50.25, clauses (a) (6) through (a)(8) are identical to Section (a)(6) through (a)(8) of the Pre-2018 Common Rule at 46.116 (See second column to the left) and therefore have been omitted here.*
Contact info	**(7)** An explanation of whom to contact for answers to pertinent questions about the research and research subjects' rights, and whom to contact in the event of a research-related injury to the subject; and		
Participation is voluntary	**(8)** A statement that participation is voluntary, refusal to participate will involve no penalty or loss of benefits to which the subject is otherwise entitled, and the subject may discontinue participation at any time without penalty or loss of benefits to which the subject is otherwise entitled.		

Basic Elements of Informed Consent			
TOPIC	**Pre-2018 Common Rule 45 CFR 46.116**	**2018 Common Rule 45 CFR 46.116(b)**	**FDA Regulations 21 CFR 50.25**
Collection of identifiable information or biospecimens	*No comparable provision in Pre 2018 Common Rule.*	**(9)** One of the following statements about any research that involves the collection of identifiable private information or identifiable biospecimens: **(i)** A statement that identifiers might be removed from the identifiable private information or identifiable biospecimens and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from the subject or the legally authorized representative, if this might be a possibility; or **(ii)** A statement that the subject's information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies.	*No comparable provision in 21 CFR Part 50.*

Additional Elements of Informed Consent			
TOPIC	**Pre-2018 Common Rule 45 CFR 46.116**	**2018 Common Rule 45 CFR 46.116(c)**	**FDA Regulations 21 CFR 50.25**
Generally	**(b)** *Additional elements of informed consent*. When appropriate, one or more of the following elements of information shall also be provided to each subject:	**(c)** *Additional elements of informed consent.* **Except as provided in paragraph (d), (e), or (f) of this section,** one or more of the following elements of information, when appropriate, shall also be provided to each subject **or the legally authorized representative**:	*NOTE: Section (b) of the FDA Regulations at 21 CFR 50.25, clauses (b)(1) through (b)(6) are identical to clauses (b)(1) through (b)(6) of the Pre-2018 Common Rule at 46.116 (See*

Additional Elements of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116(c)**	**FDA Regulations** **21 CFR 50.25**
Unforeseeable risks	**(1)** A statement that the particular treatment or procedure may involve risks to the subject (or to the embryo or fetus, if the subject is or may become pregnant) which are currently unforeseeable;	**(1)** *Same clause as in the Pre-2018 Common Rule.*	*second column to the left) and therefore have been omitted here.*
Termination by investigator	**(2)** Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's consent;	**(2)** Anticipated circumstances under which the subject's participation may be terminated by the investigator without regard to the subject's **or the legally authorized representative's** consent;	
Additional Costs	**(3)** Any additional costs to the subject that may result from participation in the research;	*NOTE: Section (c) of the 2018 Common Rule at 46.116, clauses (c)(3) through (c)(6) are identical to clauses (b)(3) through (b)(6) of the Pre-2018 Common Rule at 46.116 (See second column to the left) and therefore have been omitted here.*	
Consequences of withdrawal	**(4)** The consequences of a subject's decision to withdraw from the research and procedures for orderly termination of participation by the subject;		
Significant New Findings	**(5)** A statement that significant new findings developed during the course of the research which may relate to the subject's willingness to continue participation will be provided to the subject; and		
Number of subjects in the study	**(6)** The approximate number of subjects involved in the study.		
Use of biospecimens for commercial profit	*No comparable provision in the Pre-2018 Common Rule*	**(7)** A statement that the subject's biospecimens (even if identifiers are removed) may be used for commercial profit and whether the subject will or will not share in this commercial profit;	*No comparable provision in 21 CFR Part 50*

Additional Elements of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116(c)**	**FDA Regulations** **21 CFR 50.25**
Return of research results	*No comparable provision in the Pre-2018 Common Rule*	**(8)** A statement regarding whether clinically relevant research results, including individual research results, will be disclosed to subjects, and if so, under what conditions; and	*No comparable provision in 21 CFR Part 50*
Whole genome sequencing	*No comparable provision in the Pre-2018 Common Rule*	**(9)** For research involving biospecimens, whether the research will (if known) or might include whole genome sequencing (*i.e.,* sequencing of a human germline or somatic specimen with the intent to generate the genome or exome sequence of that specimen).	*No comparable provision in 21 CFR Part 50*
Elements of Broad Consent	*No comparable provision in the Pre-2018 Common Rule*	**45 CFR 46.116(d)** – For Elements of Broad Consent, see page 28. Note that the NIH is not implementing Broad Consent at this time.	*No comparable provision in 21 CFR Part 50*
Clinicaltrials.gov requirements	*No comparable provision in the Pre-2018 Common Rule*	*No comparable provision in the 2018 Common Rule*	**(c)** When seeking informed consent for applicable clinical trials, as defined in 42 U.S.C. 282(j)(1)(A), the following statement shall be provided to each clinical trial subject in informed consent documents and processes. This will notify the clinical trial subject that clinical trial information has been or will be submitted for inclusion in the clinical trial registry databank under paragraph (j) of section 402 of the Public Health Service Act. The statement is: "A description of this clinical trial will be available on *http://www.ClinicalTrials.gov,* as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time."

Additional Elements of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116(c)**	**FDA Regulations** **21 CFR 50.25**
Preemption of law that requires additional information	**(e)** The informed consent requirements in this policy are not intended to preempt any applicable federal, state, or local laws which require additional information to be disclosed in order for informed consent to be legally effective.	**(i)** The informed consent requirements in this policy are not intended to preempt any applicable Federal, state, or local laws **(including tribal laws passed by the official governing body of an American Indian or Alaska Native tribe) that** require additional information to be disclosed in order for informed consent to be legally effective. 45 CFR 46.116(i)	*NOTE: Section (d) of the FDA Regulations at 21 CFR 50.25 is identical to Section (e) of the Pre-2018 Common Rule (See second column to the left) and therefore has been omitted here.*
Emergency medical care	**(f)** Nothing in this policy is intended to 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.45 CFR 46.116(f)	**(j)** Nothing in this policy is intended to 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).**45 CFR 46.116(j)	**(e)** Nothing in **these regulations** is intended to 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.21 CFR 50.25(e)
Screening, recruiting or eligibility determinations	*No comparable provision in Pre 2018 Common Rule*	**(g)** *Screening, recruiting, or determining eligibility.* An IRB may approve a research proposal in which an investigator will obtain information or biospecimens for the purpose of screening, recruiting, or determining the eligibility of prospective subjects without the informed consent of the prospective subject or the subject's legally authorized representative, if either of the following conditions are met: **(1)** The investigator will obtain information through oral or written communication with the prospective subject or legally authorized representative, or **(2)** The investigator will obtain identifiable private information or identifiable biospecimens by accessing records or stored identifiable biospecimens.	*No comparable provision in 21 CFR Part 50*

Additional Elements of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116(c)**	**FDA Regulations** **21 CFR 50.25**
Posting of clinical trial consent form	*No comparable provision in Pre 2018 Common Rule*	**(h)** *Posting of clinical trial consent form.* **(1)**For each clinical trial conducted or supported by a Federal department or agency, one IRB-approved informed consent form used to enroll subjects must be posted by the awardee or the Federal department or agency component conducting the trial on a publicly available Federal Web site that will be established as a repository for such informed consent forms. **(2)** If the Federal department or agency supporting or conducting the clinical trial determines that certain information should not be made publicly available on a Federal Web site (*e.g.* confidential commercial information), such Federal department or agency may permit or require redactions to the information posted. **(3)** The informed consent form must be posted on the Federal Web site after the clinical trial is closed to recruitment, and no later than 60 days after the last study visit by any subject, as required by the protocol. **Note:** Per Policy 301: For clinical trials as defined by, and subject to, the 2018 Common Rule, if the NIH is the only site, or in the case of multi-center research when NIH is the lead site, then the NIH PI, or the PI's IC, must post one blank copy of an IRB-approved informed consent document used to enroll subjects in the research, on a publicly available federal website that is established as a repository for such informed consent documents (e.g., ClinicalTrials.gov or Regulations.gov).	*No comparable provision in 21 CFR Part 50*

Waiver or Alteration of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116**	**FDA Regulations** **21 CFR 50**
General - waiver or alteration for public benefit and service programs - 45 CFR 46.116(a)	*No comparable provision in the Pre-2018 Common Rule. See item (c) below.*	**(a)** Waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials is described in paragraph (e) of this section. General waiver or alteration of informed consent is described in paragraph (f) of this section.	*No comparable provision in 21 CFR Part 50*
Waiver or alteration for public benefit and service programs - 45 CFR 46.116(e)	*See item (c) below.*	**(e)** *Waiver or alteration of consent in research involving public benefit and service programs conducted by or subject to the approval of state or local officials—* **(1)** *Waiver.* An IRB may waive the requirement to obtain informed consent for research under paragraphs (a) through (c) of this section, provided the IRB satisfies the requirements of paragraph (e)(3) of this section. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (d) of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens. ***NOTE:*** *The NIH is not implementing Broad consent at this time.*	*No comparable provision in 21 CFR, Part 50*

Waiver or Alteration of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116**	**FDA Regulations** **21 CFR 50**
Alteration of research involving public benefit and service programs	*See item (c) below.*	**(e)(2)** ***Alteration.*** An IRB may approve a consent procedure **that omits some**, or alters some or all, of the elements of informed consent set forth **in paragraphs (b) and (c) of this section** provided the IRB **satisfies the requirements of paragraph (f)(3) of this section. An IRB may not omit or alter any of the requirements described in paragraph (a) of this section.**	*No comparable provision in 21 CFR, Part 50*
Requirements for waiver and alteration of research involving public benefit and service programs	**(c)** An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth above, or waive the requirement to obtain informed consent provided the IRB finds and documents that: **(1)** The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: **(i)** public benefit or service programs; **(ii)** procedures for obtaining benefits or services under those programs; **(iii)** possible changes in or alternatives to those programs or procedures; or **(iv)** possible changes in methods or levels of payment for benefits or services under those programs; and **(2)** The research could not practicably be carried out without the waiver or alteration.	**(e)(3)** ***Requirements for waiver and alteration.*** **In order for an IRB to waive or alter consent as described in this subsection, the IRB must find and document that:** **(i)** The research or demonstration project is to be conducted by or subject to the approval of state or local government officials and is designed to study, evaluate, or otherwise examine: **(A)** Public benefit or service programs; **(B)** Procedures for obtaining benefits or services under those programs; **(C)** Possible changes in or alternatives to those programs or procedures; or **(D)** Possible changes in methods or levels of payment for benefits or services under those programs; and **(ii)** The research could not practicably be carried out without the waiver or alteration.	*No comparable provision in 21 CFR, Part 50*

Waiver or Alteration of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116**	**FDA Regulations** **21 CFR 50**
General requirements for Waiver and Alteration	**(d)** An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that: **(1)** The research involves no more than minimal risk to the subjects; **(2)** The waiver or alteration will not adversely affect the rights and welfare of the subjects; **(3)** The research could not practicably be carried out without the waiver or alteration; and **(4)** Whenever appropriate, the subjects will be provided with additional pertinent information after participation.	**(f)(3)** ***Requirements for waiver and alteration.*** **In order for an IRB to waive or alter consent as described in this subsection, the IRB must find and document that:** **(i)** The research involves no more than minimal risk to the subjects; **(ii)** The research could not practicably be carried out without the requested waiver or alteration; **(iii) If the research involves using identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format;** **(iv)** The waiver or alteration will not adversely affect the rights and welfare of the subjects; and **(v)** Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.	*No comparable provision in 21 CFR, Part 50.* *See also 21 CFR Part 50.24 Exception from informed consent requirements for emergency research.*

Waiver or Alteration of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116**	**FDA Regulations** **21 CFR 50**
FDA Regulations **21 CFR 50.23**	*No comparable provision in the Pre-2018 Common Rule.*	*No comparable provision in the 2018 Common Rule.*	**(a)** The obtaining of informed consent shall be deemed feasible unless, before use of the test article (except as provided in paragraph (b) of this section), both the investigator and a physician who is not otherwise participating in the clinical investigation certify in writing all of the following: **(1)** The human subject is confronted by a life-threatening situation necessitating the use of the test article. **(2)** Informed consent cannot be obtained from the subject because of an inability to communicate with, or obtain legally effective consent from, the subject. **(3)** Time is not sufficient to obtain consent from the subject's legal representative. **(4)** There is available no alternative method of approved or generally recognized therapy that provides an equal or greater likelihood of saving the life of the subject. **(b)** If immediate use of the test article is, in the investigator's opinion, required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (a) of this section in advance of using the test article, the determinations of the clinical investigator shall be made and, within 5 working days after the use of the article, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. **(c)** The documentation required in paragraph (a) or (b) of this section shall be submitted to the IRB within 5 working days after the use of the test article. ***NOTE:*** *Waiver or alter elements of informed consent for non-emergency, minimal risk research is permitted in accordance with applicable FDA guidance: Guidance for Sponsors, Investigators, and Institutional Review Boards - IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects*

Waiver or Alteration of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.116**	**2018 Common Rule** **45 CFR 46.116**	**FDA Regulations** **21 CFR 50**
Alteration of Broad Consent	*No comparable provision in the Pre-2018 Common Rule*	**(e)(2)** If a broad consent procedure is used, an IRB may not omit or alter any of the elements required under paragraph (d) of this section.	*No comparable provision in 21 CFR, Part 50*
General waiver or alteration of consent - Limitation on waiver of Broad Consent Waiver when a subject refuses to consent (45 CFR 46.116(f))	*No comparable provision in the Pre-2018 Common Rule*	**(f)** *General waiver or alteration of consent* **-(1)** *Waiver.* An IRB may waive the requirement to obtain informed consent for research under paragraphs (a) through (c) of this section, provided the IRB satisfies the requirements of paragraph (f)(3) of this section. If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (d) of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens. ***Note:*** *For public benefit research see also 45 CFR 46.116(e) on page 12 above.*	*No comparable provision in 21 CFR, Part 50. However see 21 CFR 50.23 above.*

Documentation of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.117**	**2018 Common Rule** **45 CFR 46.117**	**FDA Regulations** **21 CFR 50.27**
Informed Consent should be documented	**(a)** Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative. A copy shall be given to the person signing the form.	**(a)** Except as provided in paragraph (c) of this section, informed consent shall be documented by the use of a written informed consent form approved by the IRB and signed **(including in an electronic format)** by the subject or the subject's legally authorized representative. A written copy shall be given to the person signing the **informed consent** form.	***NOTE:*** *Clauses (a) through (c)(2) of Section 50.27 of the FDA Regulations at 21 CFR 50.27 are identical to clauses (a) through (c)(2) of the Pre-2018 Common Rule at 45 CFR 46.116 (See second column to the left) and therefore has been omitted here.*
Written Consent	**(b)** Except as provided in paragraph (c) of this section, the consent form may be either of the following: **(1)** A written consent document that embodies the elements of informed consent required by §46.116. This form may be read to the subject or the subject's legally authorized representative, but in any event, the investigator shall give either the subject or the representative adequate opportunity to read it before it is signed; or	**(b)** Except as provided in paragraph (c) of this section, the informed consent form may be either of the following: **(1)** A written informed consent form that **meets the requirements of** §46.116. **The investigator shall give either the subject or the subject's legally authorized representative adequate opportunity to read the informed consent form before it is signed; alternatively,** this form may be read to the subject or the subject's legally authorized representative.	

Documentation of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.117**	**2018 Common Rule** **45 CFR 46.117**	**FDA Regulations** **21 CFR 50.27**
Short Form Consent	**(2)** A short form written consent document stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Also, the IRB shall approve a written summary of what is to be said to the subject or the representative. Only the short form itself is to be signed by the subject or the representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or the representative, in addition to a copy of the short form.	**(2)** A short form written informed consent **form** stating that the elements of informed consent required by §46.116 have been presented orally to the subject or the subject's legally authorized representative**, and that the key information required by §46.116(a)(5)(i) was presented first to the subject, before other information, if any, was provided**. The IRB shall approve a written summary of what is to be said to the subject or the legally authorized representative. When this method is used, there shall be a witness to the oral presentation. Only the short form itself is to be signed by the subject or the **subject's legally authorized** representative. However, the witness shall sign both the short form and a copy of the summary, and the person actually obtaining consent shall sign a copy of the summary. A copy of the summary shall be given to the subject or **the subject's legally authorized** representative, in addition to a copy of the short form.	

Documentation of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.117**	**2018 Common Rule** **45 CFR 46.117**	**FDA Regulations** **21 CFR 50.27**
Waiver of signed consent	**(c)** An IRB may waive the requirement for the investigator to obtain a signed consent form for some or all subjects if it finds either: **(1)** That the only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; or **(2)** That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context	**(c)(1)** An IRB may waive the requirement for the investigator to obtain a signed informed consent form for some or all subjects if it finds **any of the following**: **(i)** That the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject **(or legally authorized representative)** will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern**.** **(ii)** That the research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context**; or**	*No comparable provision in 21 CFR Part 50*
Appropriate alternative mechanism for documenting consent	*No comparable provision in Pre 2018 Common Rule*	**(iii)** If the subjects or legally authorized representatives are members of a distinct cultural group or community in which signing forms is not the norm, that 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.	*No comparable provision in 21 CFR Part 50*
Provision of written statement to subjects when documentation is waived	**(c)** In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.	**(2)** In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects **or legally authorized representatives** with a written statement regarding the research.	*No comparable provision in 21 CFR Part 50*

Documentation of Informed Consent			
TOPIC	**Pre-2018 Common Rule** **45 CFR 46.117**	**2018 Common Rule** **45 CFR 46.117**	**FDA Regulations** **21 CFR 50.27**
Exempt research: Broad consent documentation or waiver	*No comparable provision in the pre-2018 Common Rule*	(8) Secondary research for which broad consent is required: Research involving the use of identifiable private information or identifiable biospecimens for secondary research use, if the following criteria are met: **(i)** Broad consent for the storage, maintenance, and secondary research use of the identifiable private information or identifiable biospecimens was obtained in accordance with §46.116(a)(1) through (4), (a)(6), and (d);	*No comparable provision in 21 CFR Part 50*
Documentation of Broad Consent **45 CFR 46.104(d)(8)(ii)**	*No comparable provision in the pre-2018 Common Rule*	Documentation of informed consent or waiver of documentation of consent was obtained in accordance with §46.117;	*No comparable provision in 21 CFR Part 50*

Pregnant Women, Fetuses and Neonates	
Pre-2018 Common Rule	*The pre-2018 Common Rule Subpart A included pregnant women in three paragraphs listing potentially vulnerable populations: §46.107, §46.111(a)(3), and §46.111(b). The 2018 Common Rule removed pregnant woman from the list of potential vulnerable populations described in these paragraphs.* *However, no changes were made to Subpart B – Additional Protections for Pregnant Women, Human Fetuses and Neonates involved in Research (45 CFR 46.201 – 46.207). Information shown below is from the 2018 Common Rule and is identical to the Pre-2018 Common Rule*
FDA Regulations	*There are no comparable provisions in 21 CFR Parts 50 or 56*
2018 Common Rule	*The following information is taken from the 2018 Common Rule 45 CFR 46, Part B*
Applicability	**(a)** Except as provided in paragraph (b) of this section, this subpart applies to all research involving pregnant women, human fetuses, neonates of uncertain viability, or nonviable neonates conducted or supported by the Department of Health and Human Services (DHHS). This includes all research conducted in DHHS facilities by any person and all research conducted in any facility by DHHS employees. **(b)** The exemptions at §46.101(b)(1) through (6) are applicable to this subpart. **(c)** The provisions of §46.101(c) through (i) are applicable to this subpart. Reference to State or local laws in this subpart and in §46.101(f) is intended to include the laws of federally recognized American Indian and Alaska Native Tribal Governments. **(d)** The requirements of this subpart are in addition to those imposed under the other subparts of this part. 45 CFR 46.201
Definitions	The definitions in §46.102 shall be applicable to this subpart as well. In addition, as used in this subpart: **(a)** Dead fetus means a fetus that exhibits neither heartbeat, spontaneous respiratory activity, spontaneous movement of voluntary muscles, nor pulsation of the umbilical cord. **(b)** Delivery means complete separation of the fetus from the woman by expulsion or extraction or any other means. **(c)** Fetus means the product of conception from implantation until delivery. **(d)** Neonate means a newborn. **(e)** Nonviable neonate means a neonate after delivery that, although living, is not viable. **(f)** Pregnancy encompasses the period of time from implantation until delivery. A woman shall be assumed to be pregnant if she exhibits any of the pertinent presumptive signs of pregnancy, such as missed menses, until the results of a pregnancy test are negative or until delivery. **(g)** Secretary means the Secretary of Health and Human Services and any other officer or employee of the Department of Health and Human Services to whom authority has been delegated. **(h)** Viable, as it pertains to the neonate, means being able, after delivery, to survive (given the benefit of available medical therapy) to the point of independently maintaining heartbeat and respiration. The Secretary may from time to time, taking into account medical advances, publish in the Federal Register guidelines to assist in determining whether a neonate is viable for purposes of this subpart. If a neonate is viable then it may be included in research only to the extent permitted and in accordance with the requirements of subparts A and D of this part. 45 CFR 46.202

Pregnant Women, Fetuses and Neonates	
IRB Duties – Research with pregnant women, fetuses, and neonates	In addition to other responsibilities assigned to IRBs under this part, each IRB shall review research covered by this subpart and approve only research which satisfies the conditions of all applicable sections of this subpart and the other subparts of this part. 45 CFR 46.203
Research involving pregnant women or fetuses	Pregnant women or fetuses may be involved in research if all of the following conditions are met: **(a)** Where scientifically appropriate, preclinical studies, including studies on pregnant animals, and clinical studies, including studies on nonpregnant women, have been conducted and provide data for assessing potential risks to pregnant women and fetuses; **(b)** The risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus; or, if there is no such prospect of benefit, the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge which cannot be obtained by any other means; **(c)** Any risk is the least possible for achieving the objectives of the research; **(d)** If the research holds out the prospect of direct benefit to the pregnant woman, the prospect of a direct benefit both to the pregnant woman and the fetus, or no prospect of benefit for the woman nor the fetus when risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means, her consent is obtained in accord with the informed consent provisions of subpart A of this part; **(e)** If the research holds out the prospect of direct benefit solely to the fetus then the consent of the pregnant woman and the father is obtained in accord with the informed consent provisions of subpart A of this part, except that the father's consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest. **(f)** Each individual providing consent under paragraph (d) or (e) of this section is fully informed regarding the reasonably foreseeable impact of the research on the fetus or neonate; **(g)** For children as defined in §46.402(a) who are pregnant, assent and permission are obtained in accord with the provisions of subpart D of this part; **(h)** No inducements, monetary or otherwise, will be offered to terminate a pregnancy; **(i)** Individuals engaged in the research will have no part in any decisions as to the timing, method, or procedures used to terminate a pregnancy; and **(j)** Individuals engaged in the research will have no part in determining the viability of a neonate. 45 CFR 46.204

Pregnant Women, Fetuses and Neonates	
Neonates	**(a)** Neonates of uncertain viability and nonviable neonates may be involved in research if all of the following conditions are met: **(1)** Where scientifically appropriate, preclinical and clinical studies have been conducted and provide data for assessing potential risks to neonates. **(2)** Each individual providing consent under paragraph (b)(2) or (c)(5) of this section is fully informed regarding the reasonably foreseeable impact of the research on the neonate. **(3)** Individuals engaged in the research will have no part in determining the viability of a neonate. **(4)** The requirements of paragraph (b) or (c) of this section have been met as applicable. **(b)** *Neonates of uncertain viability.* Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by this subpart unless the following additional conditions are met: **(1)** The IRB determines that: **(i)** The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, and any risk is the least possible for achieving that objective, or **(ii)** The purpose of the research is the development of important biomedical knowledge which cannot be obtained by other means and there will be no added risk to the neonate resulting from the research; and **(2)** The legally effective informed consent of either parent of the neonate or, if neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative is obtained in accord with subpart A of this part, except that the consent of the father or his legally authorized representative need not be obtained if the pregnancy resulted from rape or incest. 45 CFR 46.205
Nonviable Neonates	**(c)** *Nonviable neonates.* After delivery nonviable neonate may not be involved in research covered by this subpart unless all of the following additional conditions are met: **(1)** Vital functions of the neonate will not be artificially maintained; **(2)** The research will not terminate the heartbeat or respiration of the neonate; **(3)** There will be no added risk to the neonate resulting from the research; **(4)** The purpose of the research is the development of important biomedical knowledge that cannot be obtained by other means; and **(5)** The legally effective informed consent of both parents of the neonate is obtained in accord with subpart A of this part, except that the waiver and alteration provisions of §46.116(c) and (d) do not apply. However, if either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice to meet the requirements of this paragraph (c)(5), except that the consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice to meet the requirements of this paragraph (c)(5). 45 CFR 46.205
Viable Neonates	**(d)** *Viable neonates.* A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accord with the requirements of subparts A and D of this part. 45 CFR 46.205

Pregnant Women, Fetuses and Neonates	
Research involving, after delivery, the placenta, the dead fetus or fetal material.	**(a)** Research involving, after delivery, the placenta; the dead fetus; macerated fetal material; or cells, tissue, or organs excised from a dead fetus, shall be conducted only in accord with any applicable Federal, State, or local laws and regulations regarding such activities. **(b)** If information associated with material described in paragraph (a) of this section is recorded for research purposes in a manner that living individuals can be identified, directly or through identifiers linked to those individuals, those individuals are research subjects and all pertinent subparts of this part are applicable. 45 CFR 46.206
Research which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of pregnant women, fetuses, or neonates.	The Secretary will conduct or fund research that the IRB does not believe meets the requirements of §46.204 or §46.205 only if: **(a)** The IRB finds that the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; and **(b)** The Secretary, after consultation with a panel of experts in pertinent disciplines (for example: science, medicine, ethics, law) and following opportunity for public review and comment, including a public meeting announced in the Federal Register, has determined either: **(1)** That the research in fact satisfies the conditions of §46.204, as applicable; or **(2)** The following: **(i)** The research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of pregnant women, fetuses or neonates; **(ii)** The research will be conducted in accord with sound ethical principles; and **(iii)** Informed consent will be obtained in accord with the informed consent provisions of subpart A and other applicable subparts of this part. 45 CFR 46.207

Children		
Pre-2018 Common Rule	*There were no changes Subpart D changes in the 2018 Common Rule from the Pre 2018 Common Rule. Information shown below is from the 2018 Common Rule and is identical to the Pre-2018 Common Rule*	
TOPIC	**2018 Common Rule 45 CFR 46, Subpart D**	**FDA Regulations 21 CFR 50.55, Subpart D**
Waiver	**(c)** The exceptions, additions, and provisions for waiver as they appear in paragraphs (c) through (i) of §46.101 of subpart A are applicable to this subpart. 45 CFR 46.401	*No comparable provision in 21 CFR Part 50.55*
Definitions	The definitions in §46.102 of subpart A shall be applicable to this subpart as well. In addition, as used in this subpart: **(a)** *Children* are persons who have not attained the legal age for consent to treatments or procedures involved in the research, under the applicable law of the jurisdiction in which the research will be conducted. **(b)** *Assent* means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent. **(c)** *Permission* means the agreement of parent(s) or guardian to the participation of their child or ward in research. **(d)** *Parent* means a child's biological or adoptive parent. **(e)** *Guardian* means an individual who is authorized under applicable State or local law to consent on behalf of a child to general medical care. 45 CFR 46.402	*No comparable provision in 21 CFR Part 50.55*

Children		
Pre-2018 Common Rule	*There were no changes Subpart D changes in the 2018 Common Rule from the Pre 2018 Common Rule. Information shown below is from the 2018 Common Rule and is identical to the Pre-2018 Common Rule*	
TOPIC	**2018 Common Rule 45 CFR 46, Subpart D**	**FDA Regulations 21 CFR 50.55, Subpart D**
Requirements for permission by parents or guardians and for assent by children	**(a)** In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. **If the IRB determines** that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the **research**. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived **in accord with §46.116 of subpart A**. **(b) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with and to the extent that consent is required by §46.116 of subpart A,** that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient **for research to be conducted under §46.404 or §46.405.** Where **research is covered by §§46.406 and 46.407** and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.	**(a)** In addition to the determinations required under other applicable sections of this subpart **D**, the IRB **must** determine that adequate provisions are made for soliciting the assent of the children when in the judgment of the IRB the children are capable of providing assent. **(b)** In determining whether children are capable of providing assent, the IRB must take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in clinical investigations under a particular protocol, or for each child, as the IRB deems appropriate. **(c)** The assent of the children is not a necessary condition for proceeding with the **clinical investigation** if the IRB determines: **(1)** That the capability of some or all of the children is so limited that they cannot reasonably be consulted, or **(2)** That the intervention or procedure involved in the **clinical investigation** holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the **clinical investigation**. **(d)** Even where the IRB determines that the subjects are capable of assenting, the IRB **may still waive the assent requirement if it finds and documents that:** **(1)** The **clinical investigation involves** no more than minimal risk to the subjects; **(2)** The waiver will not adversely affect the rights and welfare of the subjects; **(3)** The clinical investigation could not practicably be carried out without the waiver; and **(4)** Whenever appropriate, the subjects will be provided with additional pertinent information after participation. **(e) In addition to the determinations required under other applicable sections of this subpart D,** the IRB must determine, in **accordance with and to the extent that consent is required under part 50,** that the permission of each child's parents or guardian is **granted**.

Children		
Pre-2018 Common Rule	*There were no changes Subpart D changes in the 2018 Common Rule from the Pre 2018 Common Rule. Information shown below is from the 2018 Common Rule and is identical to the Pre-2018 Common Rule*	
TOPIC	**2018 Common Rule 45 CFR 46, Subpart D**	**FDA Regulations 21 CFR 50.55, Subpart D**
Requirements for permission by parents or guardians and for assent by children	**(c)** In addition to the provisions for waiver contained in **§46.116 of subpart A, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with Federal, state or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.** **(d)** Permission by parents or guardians shall be documented in accordance with and to the extent required by **§46.117 of subpart A.** **(e)** When the IRB determines that assent is required, it shall also determine whether and how assent must be documented. 45 CFR 46.408	**(1)** Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for **clinical investigations** to be conducted **under §50.51 or §50.52**. **(2)** Where **clinical investigations are covered by §50.53 or §50.54 and** permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child. **(f)** Permission by parents or guardians must be documented in accordance with and to the extent required by **§50.27**. **(g)** When the IRB determines that assent is required, it must also determine whether and how assent must be documented. 21 CFR 50.55

Children		
Pre-2018 Common Rule	*There were no changes Subpart D changes in the 2018 Common Rule from the Pre 2018 Common Rule. Information shown below is from the 2018 Common Rule and is identical to the Pre-2018 Common Rule*	
TOPIC	**2018 Common Rule 45 CFR 46, Subpart D**	**FDA Regulations 21 CFR 50.55, Subpart D**
Wards	**(a)** Children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407 only if such **research is**: **(1)** Related to their status as wards; or **(2)** Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards. **(b)** If the **research** is approved under paragraph (a) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the **research** and who is not associated in any way (except in the role as advocate or member of the IRB) with the **research**, the investigator(s), or the guardian organization. 45 CFR 46.409	**(a)** Children who are wards of the State or any other agency, institution, or entity can be included in clinical investigations approved under **§50.53 or §50.54** only if such **clinical investigations** are: **(1)** Related to their status as wards; or **(2)** Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards. **(b)** If the **clinical investigation** is approved under paragraph (a) of this section, the IRB **must** require appointment of an advocate for each child who is a ward. **(1) The advocate will serve** in addition to any other individual acting on behalf of the child as guardian or in loco parentis. **(2)** One individual may serve as advocate for more than one child. **(3)** The advocate **must** be an individual who has the background and experience to act in, and agrees to act in, the best interest of the child for the duration of the child's participation in the **clinical investigation**. **(4)** The advocate must not be associated in any way (except in the role as advocate or member of the IRB) with the **clinical investigation**, the investigator(s), or the guardian organization. 21 CFR 50.56

Elements of Broad Consent[1]	
Pre-2018 Common Rule	*No comparable provision in Pre 2018 Common Rule*
FDA Regulations	*No comparable provision in 21 CFR Part 50*
2018 Common Rule 45 CFR 46.116(d)	Broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens (collected for either research studies other than the proposed research or nonresearch purposes) is permitted as an alternative to the informed consent requirements in paragraphs (b) and (c) of this section [the basic and additional elements of consent]. If the subject or the LAR is asked to provide broad consent, the following shall be provided: **(1)** The information required in paragraphs (b)(2), (b)(3), (b)(5), and (b)(8) and, when appropriate (c)(7) and (9) of this section; **(2)** A general description of the types of research that may be conducted with the identifiable private information or identifiable biospecimens. This description must include sufficient information such that a reasonable person would expect that the broad consent would permit the types of research conducted; **(3)** A description of the identifiable private information or identifiable biospecimens that might be used in research, whether sharing of identifiable private information or identifiable biospecimens might occur, and the types of institutions or researcher that might conduct research with the identifiable private information or identifiable biospecimens; **(4)** A description of the period of time that the identifiable private information or identifiable biospecimens may be stored and maintained (which period of time could be indefinite), and a description of the period of time that the identifiable private information or identifiable biospecimens may be used for research purposes (which period of time could be indefinite); **(5)** Unless the subject or LAR will be provided details about the specific research studies, a statement that they will not be informed of the details of any specific research studies that might be conducted using the subject's identifiable private information or identifiable biospecimens, including the purposes of the research, and that they might have chosen not to consent to some of those specific research to those specific research studies **(6)** Unless it is known that clinically relevant research results, including individual research results, will be disclosed to the subject in all circumstances, a statement that such results may not be disclosed to the subject; and **(7)** An explanation of whom to contact for answers to questions about the subject's rights and about storage and use of the subject's identifiable private information or identifiable biospecimens, and whom to contact in the event of a research-related harm.
2018 Common Rule 45 CFR 46.116(e)	**(e)** If an individual was asked to provide broad consent for the storage, maintenance, and secondary research use of identifiable private information or identifiable biospecimens in accordance with the requirements at paragraph (d) of this section, and refused to consent, an IRB cannot waive consent for the storage, maintenance, or secondary research use of the identifiable private information or identifiable biospecimens.

[1] NIH is not implementing broad consent at this time.

Other Waivers of Consent – INDs and Military Operations - FDA Only	
Pre-2018 Common Rule	*No comparable provision in Pre 2018 Common Rule*
2018 Common Rule	*No comparable provision in 2018 Common Rule*
FDA Regulations **21 CFR 50.23**	Exception from general requirements (d)(1**)** Under 10 U.S.C. 1107(f) the President may waive the prior consent requirement for the administration of an investigational new drug to a member of the armed forces in connection with the member's participation in a particular military operation. The statute specifies that only the President may waive informed consent in this connection and the President may grant such a waiver only if the President determines in writing that obtaining consent: Is not feasible; is contrary to the best interests of the military member; or is not in the interests of national security. The statute further provides that in making a determination to waive prior informed consent on the ground that it is not feasible or the ground that it is contrary to the best interests of the military members involved, the President shall apply the standards and criteria that are set forth in the relevant FDA regulations for a waiver of the prior informed consent requirements of section 505(i)(4) of the Federal Food, Drug, and Cosmetic Act (21 U.S.C. 355(i)(4)). Before such a determination may be made that obtaining informed consent from military personnel prior to the use of an investigational drug (including an antibiotic or biological product) in a specific protocol under an investigational new drug application (IND) sponsored by the Department of Defense (DOD) and limited to specific military personnel involved in a particular military operation is not feasible or is contrary to the best interests of the military members involved the Secretary of Defense must first request such a determination from the President, and certify and document to the President that the following standards and criteria contained in paragraphs (d)(1) through (d)(4) of this section have been met. **(i)** The extent and strength of evidence of the safety and effectiveness of the investigational new drug in relation to the medical risk that could be encountered during the military operation supports the drug's administration under an IND. **(ii)** The military operation presents a substantial risk that military personnel may be subject to a chemical, biological, nuclear, or other exposure likely to produce death or serious or life-threatening injury or illness. **(iii)** There is no available satisfactory alternative therapeutic or preventive treatment in relation to the intended use of the investigational new drug. **(iv)** Conditioning use of the investigational new drug on the voluntary participation of each member could significantly risk the safety and health of any individual member who would decline its use, the safety of other military personnel, and the accomplishment of the military mission. **(v)** A duly constituted institutional review board (IRB) established and operated in accordance with the requirements of paragraphs (d)(2) and (d)(3) of this section, responsible for review of the study, has reviewed and approved the investigational new drug protocol and the administration of the investigational new drug without informed consent. DOD's request is to include the documentation required by §56.115(a)(2) of this chapter. **(vi)** DOD has explained: **(A)** The context in which the investigational drug will be administered, e.g., the setting or whether it will be self-administered or it will be administered by a health professional; **(B)** The nature of the disease or condition for which the preventive or therapeutic treatment is intended; and

Other Waivers of Consent – INDs and Military Operations - FDA Only	
FDA Regulations **21 CFR 50.23**	**(C)** To the extent there are existing data or information available, information on conditions that could alter the effects of the investigational drug. **(vii)** DOD's recordkeeping system is capable of tracking and will be used to track the proposed treatment from supplier to the individual recipient. **(viii)** Each member involved in the military operation will be given, prior to the administration of the investigational new drug, a specific written information sheet (including information required by 10 U.S.C. 1107(d)) concerning the investigational new drug, the risks and benefits of its use, potential side effects, and other pertinent information about the appropriate use of the product. **(ix)** Medical records of members involved in the military operation will accurately document the receipt by members of the notification required by paragraph (d)(1)(viii) of this section. **(x)** Medical records of members involved in the military operation will accurately document the receipt by members of any investigational new drugs in accordance with FDA regulations including part 312 of this chapter. **(xi)** DOD will provide adequate follow up to assess whether there are beneficial or adverse health consequences that result from the use of the investigational product. **(xii)** DOD is pursuing drug development, including a timeline, and marketing approval with due diligence. **(xiii)** FDA has concluded that the investigational new drug protocol may proceed subject to a decision by the President on the informed consent waiver request. **(xiv)** DOD will provide training to the appropriate medical personnel and potential recipients on the specific investigational new drug to be administered prior to its use. **(xv)** DOD has stated and justified the time period for which the waiver is needed, not to exceed one year, unless separately renewed under these standards and criteria. **(xvi)** DOD shall have a continuing obligation to report to the FDA and to the President any changed circumstances relating to these standards and criteria (including the time period referred to in paragraph (d)(1)(xv) of this section) or that otherwise might affect the determination to use an investigational new drug without informed consent. **(xvii)** DOD is to provide public notice as soon as practicable and consistent with classification requirements through notice in the Federal Register describing each waiver of informed consent determination, a summary of the most updated scientific information on the products used, and other pertinent information. **(xviii)** Use of the investigational drug without informed consent otherwise conforms with applicable law. **(2)** The duly constituted institutional review board, described in paragraph (d)(1)(v) of this section, must include at least 3 nonaffiliated members who shall not be employees or officers of the Federal Government (other than for purposes of membership on the IRB) and shall be required to obtain any necessary security clearances. This IRB shall review the proposed IND protocol at a convened meeting at which a majority of the members are present including at least one member whose primary concerns are in nonscientific areas and, if feasible, including a majority of the nonaffiliated members. The information required by §56.115(a)(2) of this chapter is to be provided to the Secretary of Defense for further review. **(3)** The duly constituted institutional review board, described in paragraph (d)(1)(v) of this section, must review and approve: **(i)** The required information sheet; **(ii)** The adequacy of the plan to disseminate information, including distribution of the information sheet to potential recipients, on the investigational product (e.g., in forms other than written);

Other Waivers of Consent – INDs and Military Operations - FDA Only	
FDA Regulations **21 CFR 50.23**	**(iii)** The adequacy of the information and plans for its dissemination to health care providers, including potential side effects, contraindications, potential interactions, and other pertinent considerations; and **(iv)** An informed consent form as required by part 50 of this chapter, in those circumstances in which DOD determines that informed consent may be obtained from some or all personnel involved. **(4)** DOD is to submit to FDA summaries of institutional review board meetings at which the proposed protocol has been reviewed. **(5)** Nothing in these criteria or standards is intended to preempt or limit FDA's and DOD's authority or obligations under applicable statutes and regulations.

In Vitro Diagnostic Devices Exception	
Pre-2018 Common Rule	*No comparable provision in Pre 2018 Common Rule. However, there is guidance from OHRP, Research under FDA's In-vitro Device Interim Final Rule (dated June 2006) that addresses when the HHS Pre-2018 Common Rule applies when using in vitro diagnostic devices.*
2018 Common Rule	*No comparable provision in 2018 Common Rule.*
FDA Regulations **21 CFR 50.23**	**Exception from general requirements (e)(1)** Obtaining informed consent for investigational in vitro diagnostic devices used to identify chemical, biological, radiological, or nuclear agents will be deemed feasible unless, before use of the test article, both the investigator (e.g., clinical laboratory director or other responsible individual) and a physician who is not otherwise participating in the clinical investigation make the determinations and later certify in writing all of the following: **(i)** The human subject is confronted by a life-threatening situation necessitating the use of the investigational in vitro diagnostic device to identify a chemical, biological, radiological, or nuclear agent that would suggest a terrorism event or other public health emergency. **(ii)** Informed consent cannot be obtained from the subject because: **(A)** There was no reasonable way for the person directing that the specimen be collected to know, at the time the specimen was collected, that there would be a need to use the investigational in vitro diagnostic device on that subject's specimen; and **(B)** Time is not sufficient to obtain consent from the subject without risking the life of the subject. **(iii)** Time is not sufficient to obtain consent from the subject's legally authorized representative. **(iv)** There is no cleared or approved available alternative method of diagnosis, to identify the chemical, biological, radiological, or nuclear agent that provides an equal or greater likelihood of saving the life of the subject. **(2)** If use of the investigational device is, in the opinion of the investigator (e.g., clinical laboratory director or other responsible person), required to preserve the life of the subject, and time is not sufficient to obtain the independent determination required in paragraph (e)(1) of this section in advance of using the investigational device, the determinations of the investigator shall be made and, within 5 working days after the use of the device, be reviewed and evaluated in writing by a physician who is not participating in the clinical investigation. **(3)** The investigator must submit the written certification of the determinations made by the investigator and an independent physician required in paragraph (e)(1) or (e)(2) of this section to the IRB and FDA within 5 working days after the use of the device. **(4)** An investigator must disclose the investigational status of the in vitro diagnostic device and what is known about the performance characteristics of the device in the report to the subject's health care provider and in any report to public health authorities. The investigator must provide the IRB with the information required in §50.25 (except for the information described in §50.25(a)(8)) and the procedures that will be used to provide this information to each subject or the subject's legally authorized representative at the time the test results are provided to the subject's health care provider and public health authorities. **(5)** The IRB is responsible for ensuring the adequacy of the information required in section 50.25 (except for the information described in §50.25(a)(8)) and for ensuring that procedures are in place to provide this information to each subject or the subject's legally authorized representative.

In Vitro Diagnostic Devices Exception	
FDA Regulations **21 CFR 50.23**	**(6)** No State or political subdivision of a State may establish or continue in effect any law, rule, regulation or other requirement that informed consent be obtained before an investigational in vitro diagnostic device may be used to identify chemical, biological, radiological, or nuclear agent in suspected terrorism events and other potential public health emergencies that is different from, or in addition to, the requirements of this regulation

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Pre-2018 Common Rule	*No comparable provision in Pre 2018 Common Rule. However, see above, the 1996 Federal Register notice, Waiver of Informed Consent Requirements in certain Emergency Research, regarding obtaining and documenting informed consent in human subjects who are in need of emergency therapy and for whom, because of the subjects' medical condition and the unavailability of LARs of the subjects, no legally effective informed consent can be obtained.*
2018 Common Rule	*No comparable provision in 2018 Common Rule*
FDA Regulations 21 CFR 50.24	**(a)** The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve that investigation without requiring that informed consent of all research subjects be obtained if the IRB (with the concurrence of a licensed physician who is a member of or consultant to the IRB and who is not otherwise participating in the clinical investigation) finds and documents each of the following: **(1)** The human subjects are in a life-threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions. **(2)** Obtaining informed consent is not feasible because: **(i)** The subjects will not be able to give their informed consent as a result of their medical condition; **(ii)** The intervention under investigation must be administered before consent from the subjects' legally authorized representatives is feasible; and **(iii)** There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the clinical investigation. **(3)** Participation in the research holds out the prospect of direct benefit to the subjects because: **(i)** Subjects are facing a life-threatening situation that necessitates intervention; **(ii)** Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and **(iii)** Risks associated with the investigation are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity. **(4)** The clinical investigation could not practicably be carried out without the waiver. **(5)** The proposed investigational plan defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact legally authorized representatives and make this information available to the IRB at the time of continuing review. **(6)** The IRB has reviewed and approved informed consent procedures and an informed consent document consistent with §50.25. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the clinical investigation consistent with paragraph (a)(7)(v) of this section. **(7)** Additional protections of the rights and welfare of the subjects will be provided, including, at least:

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FDA Regulations **21 CFR 50.24**	**(i)** Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the clinical investigation will be conducted and from which the subjects will be drawn; **(ii)** Public disclosure to the communities in which the clinical investigation will be conducted and from which the subjects will be drawn, prior to initiation of the clinical investigation, of plans for the investigation and its risks and expected benefits; **(iii)** Public disclosure of sufficient information following completion of the clinical investigation to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results; **(iv)** Establishment of an independent data monitoring committee to exercise oversight of the clinical investigation; and **(v)** If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the clinical investigation. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review. **(b)** The IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the clinical investigation, the details of the investigation and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the clinical investigation and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into a clinical investigation with waived consent and the subject dies before a legally authorized representative or family member can be contacted, information about the clinical investigation is to be provided to the subject's legally authorized representative or family member, if feasible. **(c)** The IRB determinations required by paragraph (a) of this section and the documentation required by paragraph (e) of this section are to be retained by the IRB for at least 3 years after completion of the clinical investigation, and the records shall be accessible for inspection and copying by FDA in accordance with §56.115(b) of this chapter. **(d)** Protocols involving an exception to the informed consent requirement under this section must be performed under a separate investigational new drug application (IND) or investigational device exemption (IDE) that clearly identifies such protocols as protocols that may include subjects who are unable to consent. The submission of those protocols in a separate IND/IDE is required even if an IND for the same drug product or an IDE for the same device already exists. Applications for investigations under this section may not be submitted as amendments under §§312.30 or 812.35 of this chapter. **(e)** If an IRB determines that it cannot approve a clinical investigation because the investigation does not meet the criteria in the exception provided under paragraph (a) of this section or because of other relevant ethical concerns, the IRB must document its findings and provide these findings promptly in writing to the clinical investigator and to the sponsor of the clinical investigation. The sponsor of the clinical investigation must promptly disclose this information to FDA and to the sponsor's clinical investigators who are participating or are asked to participate in this or a substantially equivalent clinical investigation of the sponsor, **and** to other IRB's that have been, or are, asked to review this or a substantially equivalent investigation by that sponsor.

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61 Federal Register 51531	**Waiver of Informed Consent Requirements in certain Emergency Research** **SUMMARY:** The Department of Health and Human Services (HHS) is announcing the waiver of the applicability of the title 45 CFR part 46 (protection of human subjects) requirement for obtaining and documenting informed consent, for a strictly limited class of research involving activities which may be carried out in human subjects who are in need of emergency therapy and for whom, because of the subjects' medical condition and the unavailability of legally authorized representatives of the subjects, no legally effective informed consent can be obtained. However, because of special regulatory limitations relating to research involving prisoners (subpart C of 45 CFR part 46) and research involving fetuses, pregnant women, and human in vitro fertilization (subpart B of 45 CFR part 46), this waiver is inapplicable to these categories of research. **Waiver:** Pursuant to Section 46.101(i) of title 45 of the Code of Federal Regulations, the Secretary of Health and Human Services (HHS) has waived the general requirements for informed consent at 45 CFR 46.116 (a) and (b), and at 46.408, to be referred to as the ''Emergency Research Consent Waiver,'' for a class of research consisting of activities 1, each of which have met the following strictly limited conditions detailed under either (a) or (b) below: **(a)** The Institutional Review Board (IRB) responsible for the review, approval, and continuing review of the research activity has approved both the activity and a waiver of informed consent and found and documented: **(1)** that the research activity is subject to regulations codified by the Food and Drug Administration (FDA) at Title 21 CFR part 50 and will be carried out under an FDA investigational new drug application (IND) or an FDA investigational device exemption (IDE), the application for which has clearly identified the protocols that would include subjects who are unable to consent, and **(2)** that the requirements for exception from informed consent for emergency research detailed in title 21 CFR section 50.24 have been met relative to those protocols, or **(b)** The IRB responsible for the review, approval, and continuing review of the research has approved both the research and a waiver of informed consent and has found and documented that the research is not subject to regulations codified by the FDA at title 21 CFR part 50 and found and documented and reported to the Office for Protection from Research Risks, Department of Health and Human Services, that the following conditions have been met relative to the research: **(1)** The human subjects are in a life threatening situation, available treatments are unproven or unsatisfactory, and the collection of valid scientific evidence, which may include evidence obtained through randomized placebo-controlled investigations, is necessary to determine the safety and effectiveness of particular interventions. **(2)** Obtaining informed consent is not feasible because: **(i)** The subjects will not be able to give their informed consent as a result of their medical condition; **(ii)** The intervention involved in the research must be administered before consent from the subjects' legally authorized representatives is feasible; and **(iii)** There is no reasonable way to identify prospectively the individuals likely to become eligible for participation in the research.

61 Federal Register 51531	**(3)** Participation in the research holds out the prospect of direct benefit to the subjects because: **(i)** Subjects are facing a life threatening situation that necessitates intervention; **(ii)** Appropriate animal and other preclinical studies have been conducted, and the information derived from those studies and related evidence support the potential for the intervention to provide a direct benefit to the individual subjects; and **(iii)** The risks associated with the research are reasonable in relation to what is known about the medical condition of the potential class of subjects, the risks and benefits of standard therapy, if any, and what is known about the risks and benefits of the proposed intervention or activity. **(4)** The research could not practicably be carried out without the waiver. **(5)** The proposed research protocol defines the length of the potential therapeutic window based on scientific evidence, and the investigator has committed to attempting to contact a legally authorized representative for each subject within that window of time and, if feasible, to asking the legally authorized representative contacted for consent within that window rather than proceeding without consent. The investigator will summarize efforts made to contact representatives and make this information available to the IRB at the time of continuing review. **(6)** The IRB has reviewed and approved informed consent procedures and an informed consent document in accord with Sections 46.116 and 46.117 of title 45 of the Code of Federal Regulations. These procedures and the informed consent document are to be used with subjects or their legally authorized representatives in situations where use of such procedures and documents is feasible. The IRB has reviewed and approved procedures and information to be used when providing an opportunity for a family member to object to a subject's participation in the research consistent with paragraph (b)(7)(v) of this waiver. **(7)** Additional protections of the rights and welfare of the subjects will be provided, including, at least: **(i)** Consultation (including, where appropriate, consultation carried out by the IRB) with representatives of the communities in which the research will be conducted and from which the subjects will be drawn; **(ii)** Public disclosure to the communities in which the research will be conducted and from which the subjects will be drawn, prior to initiation of the research, of plans for the research and its risks and expected benefits; **(iii)** Public disclosure of sufficient information following completion of the research to apprise the community and researchers of the study, including the demographic characteristics of the research population, and its results; **(iv)** Establishment of an independent data monitoring committee to exercise oversight of the research; and (v) If obtaining informed consent is not feasible and a legally authorized representative is not reasonably available, the investigator has committed, if feasible, to attempting to contact within the therapeutic window the subject's family member who is not a legally authorized representative, and asking whether he or she objects to the subject's participation in the research. The investigator will summarize efforts made to contact family members and make this information available to the IRB at the time of continuing review. In addition, the IRB is responsible for ensuring that procedures are in place to inform, at the earliest feasible opportunity, each subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, of the subject's inclusion in the research, the details of the research and other information contained in the informed consent document. The IRB shall also ensure that there is a procedure to inform the subject, or if the subject remains incapacitated, a legally authorized representative of the subject, or if such a representative is not reasonably available, a family member, that he or she may discontinue the subject's participation at any time without penalty or loss of benefits to which the subject is otherwise entitled. If a legally authorized representative or family member is told about the research and the subject's condition improves, the subject is also to be informed as soon as feasible. If a subject is entered into research with waived consent

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61 Federal Register 51531	and the subject dies before a legally authorized representative or family member can be contacted, information about the research is to be provided to the subject's legally authorized representative or family member, if feasible. For the purposes of this waiver ''family member'' means any one of the following legally competent persons: spouses; parents; children (including adopted children); brothers, sisters, and spouses of brothers and sisters; and any individual related by blood or affinity whose close association with the subject is the equivalent of a family relationship. ***NOTES:*** *This waiver is harmonized with the FDA's regulations on this topic (see below). It requires the IRB to report to OHRP that the conditions of waiver have been met.*

Additional References

1. **Policy**

   Policy 3014-301 Informed Consent
   Policy 3014-400 Research Involving Pregnant Women, Human Fetuses and Neonates
   Policy 3014-401 Research Involving Prisoners
   Policy 3014-402 Research Involving Children
   Policy 3014-403 Research Involving Adults Who Lack Decision-making Capacity to Consent to Research Participation
   Policy 3014-500 Research Involving Drugs, Biological, and Nutritional Products
   Policy 3014-501 Research Involving FDA Regulated Devices

2. **Regulations**

   HHS: 45 CFR 46
   FDA: 21 CFR part 50
   ClinicalTrials.gov
   Regulations.gov

3. **Guidance**

   FDA - Guidance for Sponsors, Investigators, and Institutional Review Boards - IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects

   OHRP - Informed Consent FAQs

   OHRP - Use of Electronic Informed Consent: Questions and Answers

   OHSRP - Everything you need to know about consent