



12 | FEBRUARY | 2025

Recent Guidance on Clinical Research Topics and What it Means to You

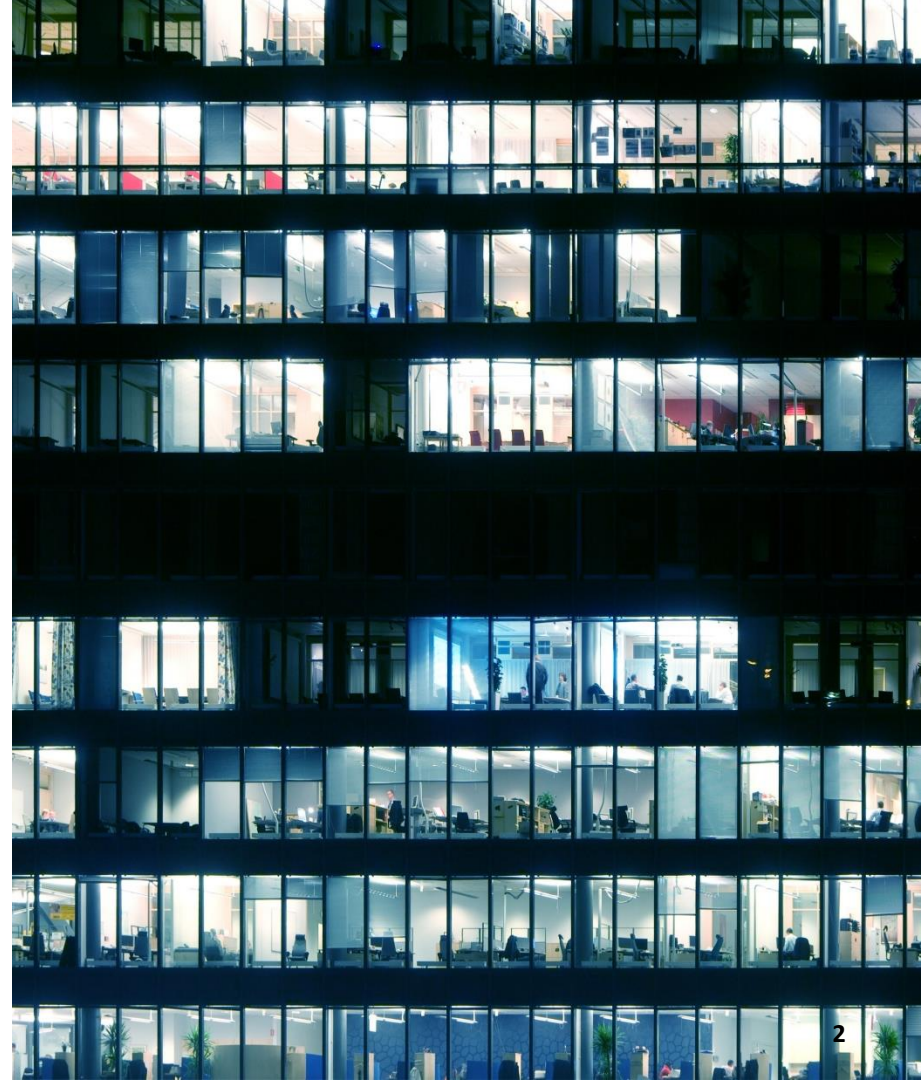
Katie Bessette

Director of Regulatory Affairs

Abbott Laboratories, Core Diagnostics

Agenda

- **Introduction:** Recent Themes and Trends
- **Final Rule #1:** Waiver of Informed Consent
- **Proposed Rule #2:** Informed Consent Form (ICF)
- **Proposed Rule #3:** Cooperative Research & Single IRB Review



Disclaimer

- This presentation represents my personal views and does not represent the position of Abbott Laboratories.
- These insights are to help guide and are not intended to be written rules on how best to achieve Regulatory approval, clearance, or otherwise.

Introduction: Recent Themes and Trends

Recent Themes and Trends

Proposals and Guidance

1. Global Regulatory Alignment

- a. US, EU, China, and rest of world have worked diligently to harmonize clinical research requirements.
- b. US regulations work in conjunction with the following EU-endorsed standards:
 - i. ICH E6 R2 – Pharma GCP
 - ii. ISO 14155 – Medical Device GCP
 - iii. ISO 20916 – IVD GCP



2. Study Design

- a. Guidance on obtaining data to support the intended use and use populations.
 - i. E.g., Better coverage across sex, race, and socio-economic status to demonstrate product performance across the intended use population ([Diversity and Sex Guidance](#))
 - ii. E.g., More stringent requirements that IVD assays have prospective data for the entire analytical range of an assay, particularly having native samples in lower and upper ranges, and not using spiked or contrived specimens, nor archived and frozen specimens.

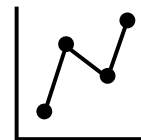


Recent Themes and Trends

Proposals and Guidance

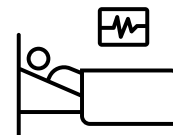
3. Data Quality

- a. Investigator oversight to assure quality of study data ([Important Deviations Guidance](#)).
- b. Use of Real World Data and Evidence particularly emphasizes expectations to assure that the data quality and fit are appropriate for the purpose ([RWD/E Guidance](#)).
 - i. Expectations of data quality (completeness, traceability, verifiability, etc.) are the same as those for a traditional prospective study.



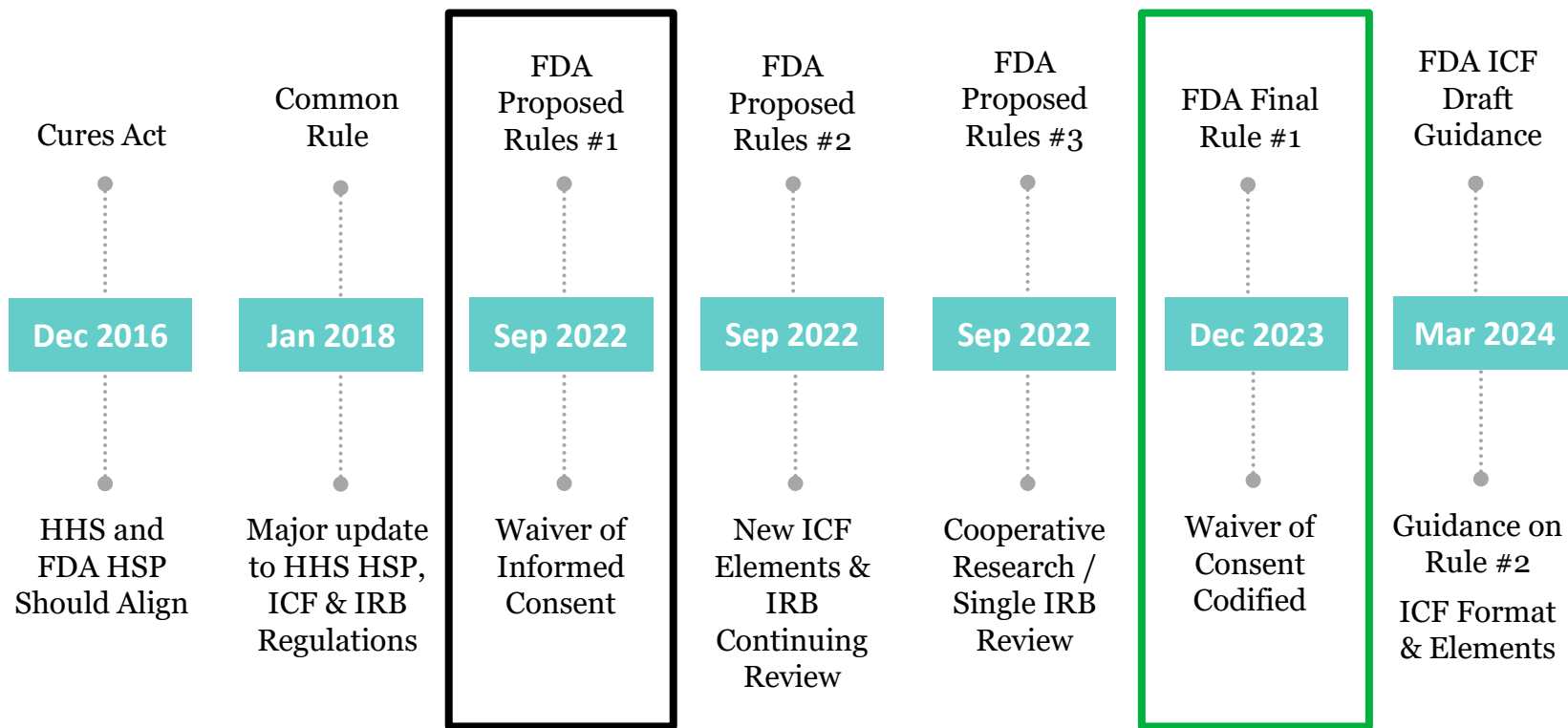
4. Patient Engagement

- a. Improving the consent process ([Understanding Consent Guidance](#))
- b. Making trial participation easier and less burdensome ([Decentralized clinical Trials \(DCT\) Guidance](#), [Patient Engagement Guidance](#)).
 - i. E.g. ways we can bring trials to where people live by having some follow up visits take place in their home (visiting nurse or virtual visit) or at their local physician office vs. going to a large academic medical center.
 - ii. E.g. let patients, care-givers and health-care providers to provide input into the study design to make it more practical, less burdensome, and more desirable to participate.



Final Rule #1: Waiver of Informed Consent

Regulatory Timeline for Congress, HHS, and FDA



Change to Regulation – Addition of 21 CFR 50.22

21 CFR 50.22 - Exception from informed consent requirements for minimal risk clinical investigations.

- The IRB responsible for the review, approval, and continuing review of the clinical investigation described in this section may approve an informed consent procedure that does not include or that alters some or all of the elements of informed consent set forth in § 50.25(a) and (b), or may waive the requirement to obtain informed consent, provided the IRB finds and documents the following:
 - a) The clinical investigation involves no more than minimal risk to the subjects;
 - b) The clinical investigation could not practicably be carried out without the requested waiver or alteration;
 - c) If the clinical investigation involves using identifiable private information or identifiable biospecimens, the clinical investigation could not practicably be carried out without using such information or biospecimens in an identifiable format;
 - d) The waiver or alteration will not adversely affect the rights and welfare of the subjects; and
 - e) Whenever appropriate, the subjects or legally authorized representatives will be provided with additional pertinent information after participation.

Regulation Impacts

21 CFR 50.20 - General requirements for informed consent

- Except as provided in 21 CFR 50.22, 50.23, and 50.24, no investigator may involve a human being as a subject in research unless the investigator has obtained the legally effective informed consent of the subject or the subject's legally authorized representative.

21 CFR 312.60 - General responsibilities of investigators

- An investigator shall obtain the informed consent of each human subject to whom the drug is administered, in accordance with Part 50 of this chapter.

21 CFR 812.2 - Applicability

- Ensures that each investigator participating in an investigation of the device obtains from each subject under the investigator's care, informed consent in accordance with Part 50 of this chapter.

Impact to Researchers

Scope:

- Most IVD device investigations fall within the scope of the rule.
- Clinical investigations involving the use, without informed consent, of previously collected biospecimens and related clinical data can play an important role in the development of new medical products.
- This rule addresses the minimal risk secondary research use of biospecimens that are **individually identifiable**.

Future Clarity:

- Industry has asked for more examples of situations when this rule would apply.
- Guidance with additional information is in process.

Key Take Away

This is a good regulation change for industry.

- Industry benefits from a waiver / alteration of informed consent when a clinical investigation poses no more than minimal risk.
 - Waiver – best case
 - Alteration – reduced burden by allowing a simplified form

NO CHANGES: IRB Review and Approval Requirements



The regulation changes do not waive or change the requirements for **IRB review** for any studies, particularly studies which use bio-specimens, whether identifiable or not.



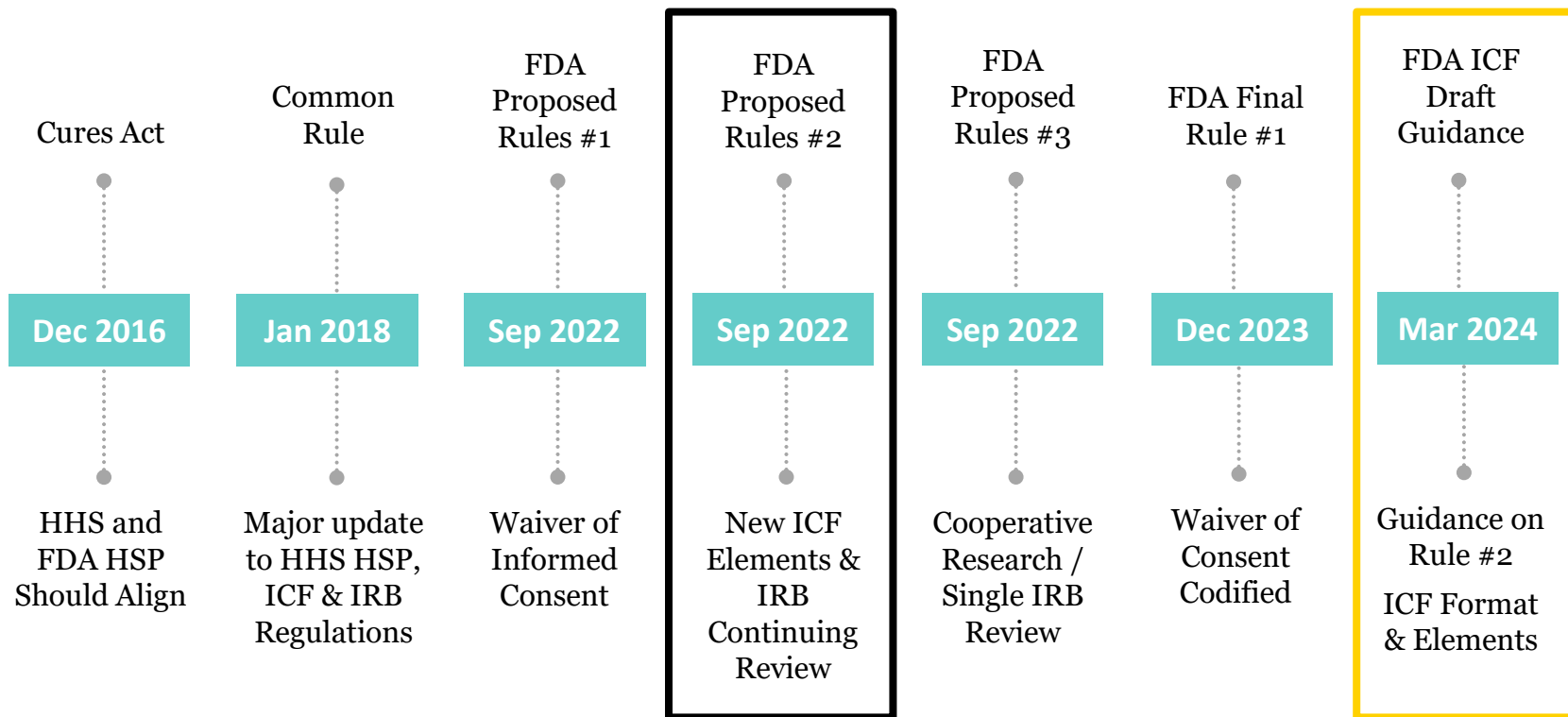
Studies which use, collect or acquire bio-specimens still must have **IRB approval**.



Studies which use identifiable data or pseudonymized data still need **IRB review**.

Proposed Rule #2: Informed Consent Forms (ICF)

Regulatory Timeline for Congress, HHS, and FDA



Proposed Changes to 21 CFR 50

(Protection of Human Subjects)

21 CFR 50.3 - Definitions

- Add a definition of “private information”
- Add a definition of “identifiable private information”
- Add a definition of “identifiable biospecimen”

21 CFR 50.20 - General requirements for informed consent

- Summary Section
- Simply plain language

21 CFR 50.25 - Elements of informed consent

- Use of data or biospecimens in future research
- Potential of commercial profit & subject’s share (or not) in profit
- Approach to sharing research results with subjects
- If whole genome sequencing will be conducted
- LAR language and when appropriate equivalence to subject
- Federal, State and Local Law is inclusive of Tribal Law and any consent considerations

Draft Guidance

(Key Information Facilitating Understanding in Informed Consent, March 2024)

Proposal:

1. Additional information required in the consent form:
 - Flexible approaches to providing key information
 - Identify key information about basic and additional elements of informed consent
 - Supplemental information that could be included
 - Recommendations to facilitate understanding
2. To simplify consent forms to make them easier to understand.”
 - “Bubble” format presentation (image to the right)

Title: A trial to evaluate the use of product X to treat health condition Y

Key Information You Should Know Before Agreeing to Participate

The key information that follows can help you learn more about this clinical trial. It can also help you decide whether or not to take part in the trial. **Please read the entire consent form or have someone read it with you.** If there is anything that you do not understand, please talk to the trial doctor or team to have your questions answered before signing the consent form.

Voluntary Participation and Right to Discontinue Participation

We are asking you to consent to participate in this research study. Your participation is voluntary and should be based on what is important to you. It is your choice to participate in this trial. If you agree to participate, you may leave at any time without penalty or loss of benefits to which you are otherwise entitled.

Purpose of the Research

The purpose of the trial is to find out if product X, the product that is being studied, is safe and effective in treating adults like you who have health condition Y.

Key Reasonably Foreseeable Risks and Discomforts (see page #)

- If you take product X, you have a chance of side effects, such as fever or rash.
- Nausea or vomiting may be related to your health condition and is a rare but serious side effect of product X. If product X is suspected to cause these or other symptoms, product X may be stopped.
- We do not know if product X will help you. There is a chance that product X could worsen condition Y.
- More information on risks is available in the consent form.

Reasonably Expected Benefits (see page #)

- Prior research suggests product X may improve condition Y.
- Researchers are studying product X in this trial to learn more about whether product X will improve condition Y.
- If you are randomly assigned to take product X, product X may improve your health condition Y. If you are randomly assigned to take the inactive pill, you will not receive product X and will not benefit directly.
- By participating in this trial, you will help researchers learn how product X may help people with condition Y.

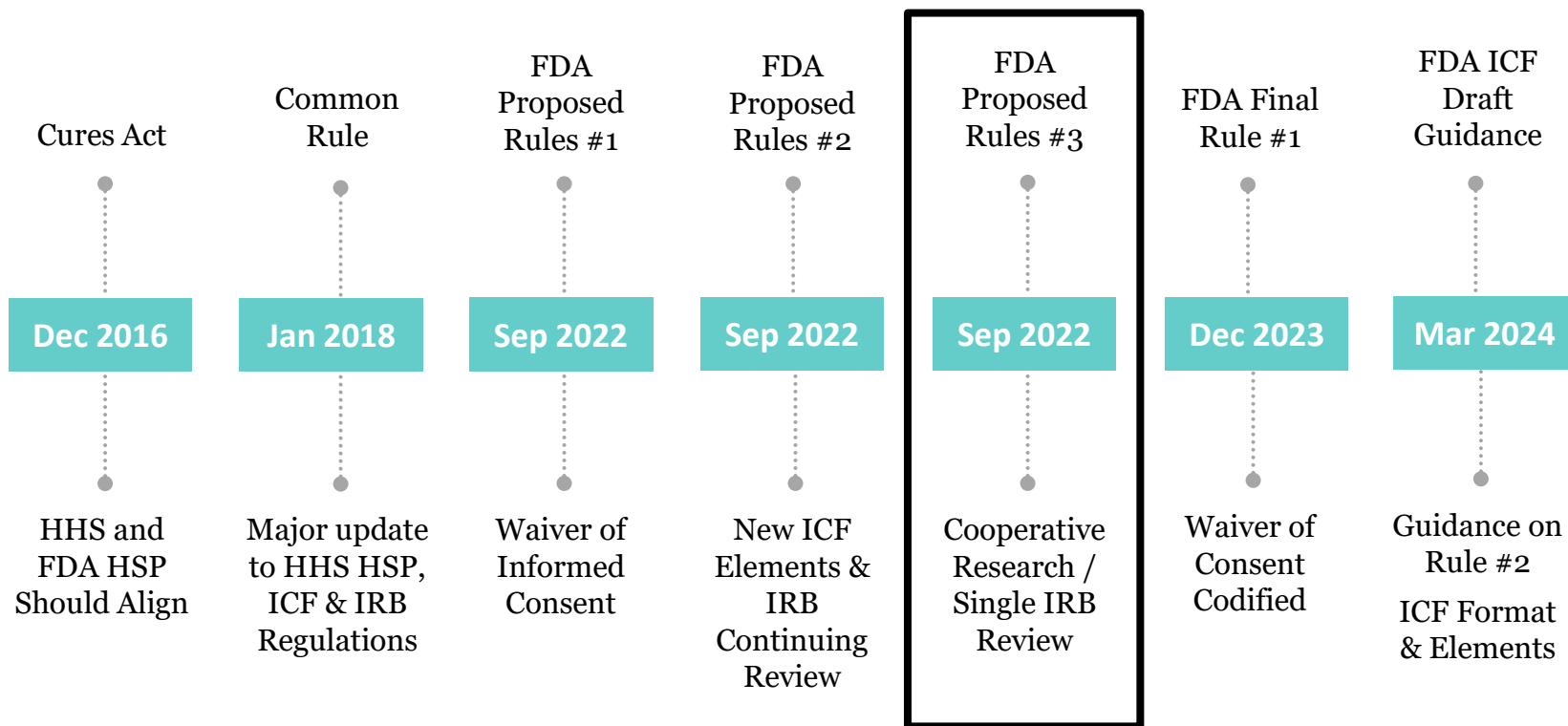
Key Take Away

This is a good regulation change for both industry and patients.

- Ensures patient understanding.
- Requires communication of more key information to facilitate patient decisions.
- Harmonizes consent requirements across U.S. regulatory bodies.

Proposed Rule #3: Cooperative Research

Regulatory Timeline for Congress, HHS, and FDA



Proposed Rule #3

Institutional Review Boards Cooperative Research

- Cooperative research involves multiple institutions working together to improve patient treatments.
- Proposal:
 - To require institutions to use a single IRB for regulated cooperative research conducted in the United States.
 - Eliminates the requirement for continuing review of some studies.
 - New recordkeeping requirements for IRBs.

Proposed Changes to 21 CFR 56

(Institutional Review Boards)

21 CFR 56.102 – Definitions & 21 CFR 56.103 – Circumstances in which IRB review is required

- Indicate consent can be written or electronic.
- Include Tribal law alongside U.S. law

21 CFR 56.107 - IRB Membership

- Add diversity requirement

21 CFR 56.109 - IRB Review of Research

- Eliminate continuing review requirement under certain circumstance
- Connect LAR rights described in 21 CFR 50

21 CFR 56.111 - Criteria for IRB approval of research

- Remove: “pregnant women, handicapped, or mentally disabled persons”
- Replace: “individuals with impaired decision-making capacity”

21 CFR 56.109 - IRB Review of Research

- Eliminate continuing review requirement under certain circumstance
- New section 21 CFR 56.109(g)

Proposed Changes to Continuing IRB Review

Proposal to adopt the provision of the common rule 45 CFR 46.109(f)(1)(iii):

- (f)(1) Unless an IRB determines otherwise, continuing review of research is not required in the following circumstances:
 - (iii) Research that has progressed to the point that it involves only one or both of the following, which are part of the IRB-approved study:
 - (A) Data analysis, including analysis of identifiable private information or identifiable biospecimens, or
 - (B) Accessing follow-up clinical data from procedures that subjects would undergo as part of clinical care.

Proposal – What is not Adopted?

Proposal not to adopt 2 other provisions of the Common Rule:

- (i) Research eligible for expedited review in accordance with [Part 46.110](#)
- (ii) Research reviewed by the IRB in accordance with the limited IRB review described in [Part 46.104\(d\)\(2\)\(iii\)](#), [\(d\)\(3\)\(i\)\(C\)](#), or [\(d\)\(7\)](#) or [\(8\)](#)

Rationale:

- Some research and/or devices on the list are non-minimal risk.
- Continuing review does add subject protections for non-minimal risk devices and studies, hence will require continuing IRB review.

Key Take Away

This is a good regulation change for industry.

- Benefits of the proposed changes:
 - Reduce administrative and coordination costs.
 - Allow cooperative research to start earlier.
 - Reduce the need to reconcile different IRB review decisions.

Thank you!