[redacted]

GUIDANCE ON THE REVISED COMMON RULE

Common Rule Bulletin# 1: Informed Consent Requirements – "Key Information"

The revised Common Rule (rCR), referred to as the "2018 requirements" or sometimes as "the Final Rule", contains several new provisions that take effect for all new protocols that receive initial approval on and after January 21, 2019. A subset of the changes affects informed consent and this document aims to provide research teams with guidance on our current understanding of the new informed consent provisions and how to operationalize them so that informed consent documents achieve the intended aim of the revisions and are compliant with the regulations.
Note: This guidance is intended for use by the [redacted] *and may be superseded by future* [redacted] *guidance or policy, or guidance issued by the Office for Human Research Protections (OHRP).*

Summary of "Key Information" Requirement

- The rCR requires informed consent to begin with *a concise and focused presentation of key information* to assist prospective subjects in understanding reasons to enroll in a protocol or not.
- These regulations do not specify what are considered "key" elements. This is, in part, to allow institutions the flexibility to develop consent forms that are tailored to the nature of the specific research study and to the type of information being provided in the consent
- OHSRP suggests that research teams whose studies are subject to the rCR provide potential research subjects with information specific to the study and, depending on the study, information that is likely to be most important to the specific persons or group(s) who may consider enrollment in the protocol.
- OHSRP currently encourages experimentation and creativity in presenting key information. A list of questions developed by the HHS Secretary's Advisory Committee on Human Research Protections (SACHRP) might help research teams consider this issue (Appendix 1 and https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-november-13-2018/index.html).
- The regulatory preamble lists 5 items that **would generally** be considered key information (but are not explicitly required as such by the regulations):
    - that consent is being sought for research and that participation is voluntary;
    - the purposes of the research, the expected duration of the prospective subject's participation, and the procedures to be followed in the research
    - the reasonably foreseeable risks or discomforts to the prospective subject;
    - the benefits to the prospective subject or to others that may reasonably be expected from the research; and
    - appropriate alternative procedures or courses of treatment, if any, that might be advantageous to the prospective subject.

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- SACHRP listed other items that **might** be key information for subjects in certain studies:
    - design features such as randomization, placebo, discontinuation of other treatments;

- how trial treatment is or is not similar to clinical care;
- significant costs of participation;
- compensation for research-related injury;
- payment;
- impact on future clinical care;
- impact on others (e.g. caregivers, family members, partners);
- post-participation access to the study drug or intervention.

Background

There have been concerns expressed within the research and IRB communities that the informed consent document has become too legalistic, which impedes one of the document's primary purposes, that is to provide the potential subject with information that would help them decide whether or not they should join a research protocol.

The new consent requirements present an opportunity to rethink how to discuss research studies with potential subjects. [redacted]'s goal is to provide each potential subject with the information needed to make a decision that is compatible with their goals and values. Rethinking the information presented and the organization of the consent document is an important step in furthering that objective.

Although there is no consensus as to what constitutes "key information", there is general agreement that it should include the information most important for a subject to make a decision about enrolling in research and be presented in a manner that fosters understanding. As much as possible, the information provided, and its organization and presentation should be considered from the perspective of the subject. OHSRP encourages research teams to engage with their subject population(s) to determine how best to identify the key information and present the consent in a way that it meets the goal of facilitating comprehension while aiding decision-making.

The main changes to the consent document required by the rCR are:

1. A requirement that informed consent begin with a concise and focused presentation of "key information" and a requirement that the consent be organized in a manner to facilitate understanding.
2. The introduction of a "reasonable person standard".
3. Additional required elements of consent.
4. Posting of consents for clinical trials.
5. Broad Consent. *This will not be addressed in this guidance, nor implemented at* [redacted] *at this time.*

This bulletin will only address the first of these.
Subsequent guidance from OHSRP will address the remaining changes.

The Key Information Section of Informed Consent Documents

The rCR contains the following new provision (45 CFR 46.116(a)):

> (5) Except for broad consent obtained in accordance with paragraph (d) of this section:
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> (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.
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> (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.

Frequently Asked Questions regarding Key Information

Does the rCR tell me what is "key" information?
The rCR does not specify what is key information and, as of this time, OHRP has not provided any official guidance on this topic. However, it is discussed in the preamble to the regulation and SACHRP spent substantial time on this topic, finalizing a recommendation at their October 2018 meeting (https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-november-13-2018/index.html). The preamble identifies 5 items that might be considered key information:

1. The fact that consent is being sought for research and that participation is voluntary
2. The purposes of the research, the expected duration of the prospective subject's participation, and the procedures to be followed in the research
3. The reasonably foreseeable risks or discomforts to the prospective subject
4. The benefits to the prospective subject or to others that may reasonably be expected from the research
5. Appropriate alternative procedures or courses of treatments, if any, that might be advantageous to the prospective subject.

While these items reflect OHRP's thinking when writing the regulation, *these elements are not required by the regulation*. For any given study, one or more of these elements may or may not be key information dependent upon the type of study and anticipated participant. For example, in a minimal risk study, risks may not constitute key information. Similarly, in a non-therapeutic study enrolling healthy volunteers, there may not be any alternatives besides not enrolling in the study. From strictly a compliance perspective, these elements might be thought of as a "safe harbor", meaning if these are included, the researcher/institution are considered by default as in

compliance. However, SACHRP has explicitly addressed this and advises not relying solely on this approach, as there may be other information not listed in the preamble that *is* key information for a particular protocol. The intent of this new requirement is to facilitate the decision making of the subject, not a check list for regulatory compliance.

How do I decide what information is "key"?
In deciding what information is "key", the PI and research team should consider not only their own perspective but should be certain to include the reasonably anticipated perspective and needs of the research subject. It is the information that is *"most likely to assist a prospective subject...in understanding the reasons why one might or might not want to participate…."*

The research team should consider the population of individuals that might consider enrolling in the protocol. Are there any special or unique features that might determine what is important to that group of people? In a multi-site study, it is possible that the populations may differ between sites, therefore the key information section may need to be tailored to individual sites and it would therefore differ between sites.

In its recent deliberations, SACHRP developed a list of questions that might be useful for investigators to think through in deciding what information might be "key information". These are appended to this document (Appendix 1).

Does "key information" differ according to study design?
Study design is one consideration that may determine what information is "key"; however, study design alone does not prescribe a certain set of information to be included. Certain elements of study design are likely to be "key", such as;

- Whether there is randomization
- Whether there is a placebo arm
- Whether subjects will have to discontinue current treatments.

What other information might be considered "key"?
In its recent letter to the HHS Secretary (https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-november-13-2018/index.html), SACHRP provided the following list of considerations that might be regarded as "key".

- How the treatment in the protocol is similar to, or different from, the clinical care the subject would receive if not in the protocol
- Any significant costs that could be incurred as a result of participation
- Compensation for injury
- How much time and/or how many research visits are required for participation
- Payments to subjects

- Impact on the subject's future clinical care. For example, whether use of an experimental intervention is likely to make a standard clinical intervention ineffective or unavailable after the study
- Potential impact on non-participants e.g., caregivers, family members, children, partners and the public at large
- Post-participation access to the experimental intervention.

For a given protocol, any one or more of the above might be important, depending on the nature of the research and the population being enrolled.

Should risk information always be included as key information? What risks should I list in this section?
While risk information is likely to be key in many protocols, there are situations where it may not be. For example, in a minimal risk study, it may not be necessary to list any risks.

Many clinical trials have extensive risk information and it is neither feasible nor advisable to list all risks in the key information section. However, risks that could be important to call out include the following:

- Those that are most severe
- Those that are most common
- Those that differ from the standard treatment that the subject would receive outside of the protocol
- Any risk that, without more information, could be considered as a criterion to decide whether or not to participate.

Risks that are listed as "key information" may be repeated in the body of the consent, so that the subject can refer to a complete list of risk information in one place.

The investigator should also consider whether potential inconveniences might be key information. For example, if participation in the protocol would limit a person's physical activity, or restrict their dietary intake.

What about benefits?
Similar to risks, potential benefits are likely to be important information that subjects may use to decide whether or not to participate. In its recent letter, SACHRP addressed this issue, including the following statement in its letter to the Secretary (https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-november-13-2018/index.html):

> "Implicit in consideration of how best to present risks of harm and potential benefits to potential subjects is the concern that patients who are potential subjects may not fully appreciate that research – even research that has some potential to benefit them directly – has the primary goal of advancing knowledge rather than delivering treatment. Discussing potential benefit may pose a particular challenge. Potential direct benefit to

subjects should not be overstated and should be distinguished from the anticipated value or societal benefit of the research in simple and straightforward terms.

SACHRP is aware that some IRBs have responded to concerns about potential subjects' overestimation of direct benefit by minimizing information about potential direct benefit in the consent form, reasoning that subjects will thus be less likely to believe that therapy and research are governed by the same primary goal of advancing the individual patient's best interest. However, because patients who are potential research subjects often approach clinical trials with the hope of direct benefit, minimal or vague language about potential direct benefit does not correct that misperception. Potential benefits are a legitimate consideration in an individual's decision to enroll; it is acceptable to include an accurate and specific description of potential benefit as key information."

Should I repeat information from the "key information" in the body of the consent?
Information may be repeated if it facilitates understanding. For example, it is unlikely that all risks or research procedures will be presented in the key information section. Repeating that information in the body of the consent would therefore allow the subject to have all pertinent information available in one place.

That said, if a complete element of consent is addressed in the "key information", it may not be necessary to repeat it later e.g., a statement that the study involves research or that participation is voluntary.

How should I organize and present the "key information"?
The regulations do not specify how the information should be presented. In some instances, a narrative or list may be most appropriate. In other examples, the investigator may wish to use tables or graphics. The regulatory requirement is that the information "must be organized and presented in a way that facilitates comprehension". OHSRP currently encourages experimentation and creativity in presenting the "key information".

Appendix I

Secretary's Advisory Committee on Human Research Protections (SACHRP) List of Questions

SACHRP developed a list of questions to help writers of consent materials and IRBs identify the key information for a given trial. The following questions may help authors of consent materials and IRBs identify the key information that a prospective subject may need in order to make a well-informed decision about whether to participate or not:

- What are the main reasons a subject *will* want to join this study?
- What are the main reasons a subject *will not* want to join this study?
- What is the research question the study is trying to answer? Why is it relevant to the subject?
- What aspects of research participation or this particular study are likely to be unfamiliar to a prospective subject, diverge from a subject's expectations, or require special attention?
- What information about the subject is being collected as part of this research?
- What are the types of activities that subjects will do in the research?
- What impact will participating in this research have on the subject outside of the research? For example, will it reduce options for standard treatments?
- How will the subjects' experience in this study differ from treatment outside of the study?
- In what ways is this research novel?

The answers to these questions can be used to help identify the appropriate key information for a given protocol. This is not an exhaustive list, and it should not be used as a checklist.