
Key Information and Facilitating Understanding in Informed Consent Guidance for Sponsors, Investigators, and Institutional Review Boards

DRAFT GUIDANCE

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Office of Clinical Policy (OCLiP)**

**U.S. Department of Health and Human Services
Office for Human Research Protections (OHRP)**

**March 2024
Procedural**

Key Information and Facilitating Understanding in Informed Consent

Guidance for Sponsors, Investigators, and Institutional Review Boards

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1 **Key Information and Facilitating Understanding**
2 **in Informed Consent**
3 **Guidance for Sponsors, Investigators, and**
4 **Institutional Review Boards¹**
5

6
7 This draft guidance, when finalized, will represent the current thinking of the Food and Drug
8 Administration (FDA or Agency) and the Office for Human Research Protections (OHRP) on this topic.
9 It does not establish any rights for any person and is not binding on FDA, OHRP, or the public. You can
10 use an alternative approach if it satisfies the requirements of the applicable statutes and regulations. To
11 discuss an alternative approach, contact the FDA or OHRP staff responsible for this guidance as listed on
12 the title page.
13

14
15
16
17 **I. INTRODUCTION**
18

19 This guidance provides recommendations on provisions of the Department of Health and Human
20 Services (HHS) regulations on the protection of human subjects as well as certain proposed
21 revisions to FDA’s current regulations for the protection of human subjects.² Specifically, this
22 guidance addresses the presentation of key information and includes recommendations for the
23 content, organization, and presentation of informed consent³ information in FDA-regulated
24 clinical investigations of drugs, devices, and biologics (collectively *medical products*) and in

¹ This guidance has been prepared by the Office of Medical Policy in the Center for Drug Evaluation and Research in cooperation with the Center for Biologics Evaluation and Research, the Center for Devices and Radiological Health, and the Office of Clinical Policy at the Food and Drug Administration, and the HHS Office for Human Research Protections.

² This guidance uses the term *human subject* or *subject* to describe individuals who participate in clinical investigations as defined by FDA’s human subject protection regulations in 21 CFR 50.3(g) and 56.102(e), or who participate in human subjects research as defined by HHS’s human subjects protection regulations in 45 CFR 46.102. We acknowledge that some interested parties may prefer other terms, such as *trial participant* and *research volunteer*, but we believe it is important to use the regulatory term in this guidance.

³ The term *consent* is subsequently used in this guidance in place of *informed consent* for brevity and plain language, unless quoting regulatory language.

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25 HHS-supported or -conducted nonexempt human subjects research.^{4,5} The recommendations in
26 this guidance should inform the communication of consent information to subjects, including
27 prospective subjects or their legally authorized representatives, and may be conveyed by written,
28 oral, or electronic means.

29
30 This guidance is intended to assist institutional review boards (IRBs), investigators, and sponsors
31 engaged in or responsible for oversight of human subject research subject to FDA and/or HHS
32 regulations with the development of consent information that would comply with 45 CFR
33 46.116(a)(5) and FDA’s proposed revisions to 21 CFR 50.20(e), if finalized as proposed.⁶ FDA-
34 regulated clinical investigations conducted or supported by HHS are subject to both HHS and
35 FDA regulations, per 45 CFR 46.101, 21 CFR 50.1, and 21 CFR 56.101.

36
37 In general, FDA’s and OHRP’s guidance documents do not establish legally enforceable
38 responsibilities. Instead, guidances describe the Agency’s current thinking on a topic and should
39 be viewed only as recommendations, unless specific regulatory or statutory requirements are
40 cited. The use of the word *should* in Agency guidances means that something is suggested or
41 recommended, but not required.

42
43

II. BACKGROUND

44
45

46 FDA’s regulations in 21 CFR parts 50 and 56 for the protection of human subjects are intended
47 to protect the rights, safety, and welfare of human subjects participating in FDA-regulated
48 clinical investigations and include requirements for informed consent and IRB review.

49

50 On January 19, 2017, HHS announced revisions to 45 CFR part 46, subpart A (the Common
51 Rule), which are known as the revised Common Rule.⁷ The revised Common Rule is intended to

⁴ This guidance applies to FDA-regulated clinical investigations of drugs, biologics, or devices that are subject to 21 CFR parts 50 and 56, including investigations under 21 CFR parts 312 and 812. This guidance also applies to HHS-supported or -conducted nonexempt human subjects research that is subject to 45 CFR part 46. As used in this guidance, an *investigational medical product* is an investigational drug or biological product as defined in 21 CFR part 312 or an investigational device as defined in 21 CFR part 812.

⁵ In this guidance, the terms *investigation*, *trial*, *study*, and *research* are used interchangeably and refer to clinical investigations regulated by FDA under 21 CFR parts 50 and 56 and to human subjects research subject to regulation by HHS under 45 CFR part 46, as applicable, unless otherwise noted.

⁶ See FDA’s notice of proposed rulemaking “Protection of Human Subjects and Institutional Review Boards” (87 FR 58733, September 28, 2022), available at <https://www.federalregister.gov/documents/2022/09/28/2022-21088/protection-of-human-subjects-and-institutional-review-boards>. As stated in the preamble, FDA intends to exercise enforcement discretion with respect to the proposed revisions to 21 CFR 50.20(d) through (e), 50.25(a)(9) and (b)(7) through (9), and 50.27(b)(2) for FDA-regulated studies that are ongoing when the proposed new requirements would become effective. In the event the proposed rule is not finalized as proposed, FDA intends to address any differences in future guidance.

⁷ In this guidance, the phrase *revised Common Rule* refers to the final rule (82 FR 7149, January 19, 2017) codified in 45 CFR part 46, subpart A. It is also referred to as the 2018 Requirements. The term *harmonize* as used in

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52 better protect human subjects involved in research, while facilitating research and reducing
53 burden, delay, and ambiguity for the regulated community.⁸ Prior to the most recent revisions to
54 the Common Rule, FDA’s regulations were largely consistent with the requirements in the
55 Common Rule, with a few exceptions generally arising from differences in FDA’s mission or
56 statutory authority.

57
58 Section 3023 of the Cures Act⁹ directs the Secretary of HHS to harmonize differences between
59 HHS’s and FDA’s human subject protection regulations to the extent practicable and consistent
60 with other statutory provisions. FDA has issued a notice of proposed rulemaking (the proposed
61 rule) proposing to amend 21 CFR parts 50 and 56¹⁰ in accordance with the harmonization
62 requirement in the Cures Act.

63 64 65 III. KEY INFORMATION SECTION

66
67 The revised Common Rule requires consent information to “begin with a concise and focused
68 presentation of the key information that is most likely to assist a prospective subject or legally
69 authorized representative in understanding the reasons why one might or might not want to
70 participate in the research” (45 CFR 46.116(a)(5)(i)). FDA’s proposed regulations would add
71 identical language to 21 CFR 50.20(e)(1).

72
73 The presentation of key information at the beginning of the consent process can help facilitate
74 discussions between a prospective subject and an investigator about whether the prospective
75 subject should participate in the trial. This information also may be useful to enrolled subjects as
76 a resource and to facilitate any further discussions with investigators. We recommend that the
77 key information section of a consent document¹¹ be relatively short (e.g., generally no more than
78 a few pages). A sample key information section of a consent form for a hypothetical clinical trial
79 is included in the appendix of this guidance. The format of the sample is based, in part, on
80 research regarding how the presentation of information may affect consumers’ understanding of

FDA’s proposed rule and in this guidance means “harmonize to the extent practicable and consistent with other statutory provisions,” consistent with section 3023 of the 21st Century Cures Act (Cures Act) (Public Law 114-255). Some HHS-supported or -conducted research is not subject to the revised Common Rule per 45 CFR 46.101(l)(3) and is not required to address the provisions of the revised Common Rule addressed in this guidance.

⁸ 82 FR 7149 (January 19, 2017).

⁹ Public Law 114-255.

¹⁰ See footnote 6. FDA previously has indicated in guidance that the provisions in the revised Common Rule related to the content, organization, and presentation of information included in the consent form and process are not inconsistent with FDA’s current policies and guidances. See the guidance for sponsors, investigators, and institutional review boards *Impact of Certain Provisions of the Revised Common Rule on FDA-Regulated Clinical Investigations* (October 2018). We update guidances periodically. For the most recent version of a guidance, check the FDA guidance web page at <https://www.fda.gov/regulatory-information/search-fda-guidance-documents>.

¹¹ In this guidance, the terms *informed consent form* and *informed consent document* are used interchangeably.

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81 information found in labeling for prescription drugs.¹² Our recommendations in this guidance
82 are not requirements, but are intended to provide considerations for how to present key
83 information to prospective subjects.
84

85 For studies using a short form written consent in conjunction with an oral presentation of
86 informed consent, the revised Common Rule at 45 CFR 46.117(b)(2) requires, and FDA’s
87 regulation at 21 CFR 50.27(b)(2) (if the rule is finalized as proposed) would require, that the key
88 information be presented to a prospective subject or their legally authorized representative at the
89 beginning of the informed consent process, before other information. Additionally, consent
90 documents developed for FDA-regulated clinical investigations allowed to proceed under 21
91 CFR 50.24 (“Exception From Informed Consent Requirements for Emergency Research”) would
92 also be required to begin with a key information section.¹³ Similarly, consent documents
93 developed for expanded access use of an investigational drug would be required to begin with a
94 key information section (21 CFR 312.305(c)(4)).
95

A. Flexible Approaches to Providing Key Information

96
97
98 There are multiple strategies for providing key information to prospective research subjects that
99 would be consistent with the provisions of the revised Common Rule and FDA’s proposed rule.
100 Interested parties may consider developing an approach that encompasses principles from a
101 variety of sources for the key information section, depending on the distinctive attributes and
102 design of the study, the prospective subject population, the condition being examined, and other
103 relevant factors. We encourage interested parties to develop innovative ways and utilize
104 available technologies to provide key information that will help prospective subjects better
105 understand the reasons why one might or might not want to participate in the research.
106 Interested parties could consider developing alternate ways to present key information that would
107 facilitate understanding by prospective subjects by, for example, consulting in advance with
108 patient advocacy groups or prospective subjects about their views on key information. The key
109 information section could also be presented using alternative media, such as illustrations, video,
110 and electronic tablets, to meet the goals of improving clarity and increasing prospective subjects’
111 understanding of consent information.
112

¹² Boudewyns, V, AC O’Donoghue, B Kelly, SL West, O Oguntimein, CM Bann, and LA McCormack, 2015, Influence of Patient Medication Information Format on Comprehension and Application of Medication Information: A Randomized, Controlled Experiment, *Patient Educ Couns*, 98(12):1592–1599, doi: 10.1016/j.pec.2015.07.003.

¹³ Proposed 21 CFR 50.24(a)(6) (87 FR 58733 at 58749, September 28, 2022) would require an IRB to approve a consent document that meets the requirements of part 50 (including the key information provision) as a condition of authorizing an exception from informed consent requirements. See also the guidance for institutional review boards, clinical investigators, and sponsors *Exception From Informed Consent Requirements for Emergency Research* (April 2013). For research that is not FDA-regulated and is carried out under OHRP’s Emergency Research Consent Waiver provisions (61 FR 51531-51533, October 2, 1996) for research where obtaining informed consent from subjects or their legally authorized representatives is not feasible, there is no key information requirement. Where consent is feasible, the consent process and documents must satisfy the key information requirement.

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B. Identifying Key Information About Basic and Additional Elements of Informed Consent

We recommend that the key information section of the consent form begin with an introductory statement to frame the key information included in the consent form and to guide prospective subjects when reading the entire document. We do not recommend that the key information section of the consent form necessarily include each element of informed consent contained in 45 CFR 46.116(b) and (c) or in 21 CFR 50.25(a) and (b), including the proposed revisions to that section.¹⁴

One approach to developing the content of the key information section is for prospective subjects and other interested parties to advise on which basic and additional elements of informed consent may be considered “key” from the perspective of prospective subjects for a particular study. We recommend that the most important elements for a particular study be included at the beginning of the key information section.

Which basic and additional consent elements should be included in the key information section may vary based on factors such as the study attributes and its design; the condition(s), behavior(s), or outcome(s) being examined; and the prospective subject population. Basic and additional elements (or parts of such elements) of informed consent that are not addressed (or not fully addressed) in the key information section would need to be included elsewhere in the consent form as required (21 CFR 50.25(a) and (b) and 45 CFR 46.116(b) and (c)).

If appropriate, the elements of informed consent that are addressed in the key information section can also be repeated in other parts of the consent form. For instance, information about the most important reasonably foreseeable risks (e.g., most serious and/or most common adverse events) could be addressed in the key information section and could also be repeated with comprehensive risk information later in the consent form. Appropriate repetition of key information, particularly for longer and more-complex consent forms, can help clarify concepts and ensure that the entire consent form remains understandable to prospective subjects. We suggest using page numbers (or hyperlinks for electronic consent forms) to cross-reference information from the key information section to other sections of the consent form.¹⁵ When the key information section encompasses all information for a required consent element (21 CFR 50.25(a) and (b) and 45 CFR 46.116(b) and (c)), further discussion regarding that element may not be needed in the remainder of the consent form.

Certain studies, such as those involving no more than minimal risk, may have relatively brief consent forms. In such cases, the key information section could constitute the majority of or

¹⁴ For a full discussion of how to address the elements of informed consent during the informed consent process, see the FDA guidance for IRBs, clinical investigators, and sponsors *Informed Consent* (August 2023).

¹⁵ The terms *form* and *document* are not intended to discourage the use of electronic media and other innovative approaches to improving the consent form and process. For more information on electronic informed consent, see the FDA and OHRP joint guidance for institutional review boards, investigators, and sponsors *Use of Electronic Informed Consent: Questions and Answers* (December 2016).

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151 even the entire consent document. This approach may be acceptable as long as the entire consent
152 document provides sufficient information to help prospective subjects make an informed
153 decision about participation and the document includes all of the required elements of informed
154 consent described in 21 CFR 50.25(a) and (b) and 45 CFR 46.116(b) and (c). If the entire
155 consent form is the key information section, it does not need to be labeled “key information.”
156

157 Our recommendations on how to address basic and additional elements of informed consent in
158 the key information section are discussed in the topics that follow. These specific topics were
159 selected because, in our view, these topics are likely to be considered key information for FDA-
160 regulated clinical investigations and HHS-supported or -conducted nonexempt human subjects
161 research. Some elements of informed consent, such as information regarding confidentiality of
162 subject records under 21 CFR 50.25(a)(5) and 45 CFR 46.116(b)(5), are not addressed in this
163 guidance, although they may be considered key information for some study designs.
164

165 The following topics, including the sample approach in the appendix, are intended to provide
166 suggestions that we believe can help interested parties conducting research present key
167 information in a concise and focused way that facilitates comprehension.¹⁶
168

169 *1. Voluntary Participation and Right to Discontinue Participation*¹⁷ 170

171 A statement that consent for research is being sought and that participation is voluntary is a
172 required element of informed consent, and we recommend that this element be included as key
173 information. We recommend including a statement as part of key information that a prospective
174 subject’s decision not to participate in the study or to discontinue participation at any time will
175 involve no penalty or loss of benefits to which the prospective subject is otherwise entitled. In
176 some circumstances, interested parties may consider including a statement that assures
177 prospective subjects that any decision not to participate in or to withdraw their consent from a
178 study will not adversely affect their relationship(s) with or medical care received from health
179 care providers.
180

181 *2. Purpose of the Research, Expected Duration, and Procedures To Be Followed*¹⁸ 182

183 The key information section should convey information that is most likely to provide prospective
184 subjects with a clear understanding of the purpose of the study and relevant details of the
185 protocol (e.g., explaining in language understandable to prospective subjects that the study
186 design is a randomized investigation with a placebo component). This approach to key
187 information may include a simple description of why the research is being conducted and why
188 the prospective subject is being asked to participate (e.g., due to the subject’s diagnosis, the stage

¹⁶ See, e.g., Freer, Y, N McIntosh, S Teunisse, KJS Anand, and EM Boyle, 2009, More Information, Less Understanding: A Randomized Study on Consent Issues in Neonatal Research, *Pediatrics*, 123(5):1301, doi: 10.1542/peds.2007-3860.

¹⁷ 21 CFR 50.25(a)(8) and 45 CFR 46.116(b)(8).

¹⁸ 21 CFR 50.25(a)(1) and 45 CFR 46.116(b)(1).

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189 or status of their health condition, their lack of response to previous treatments, or other factors,
190 such as inclusion of prospective subjects from different racial groups, ethnicities, gender
191 identities, or socioeconomic status). The information should be explained in a way that promotes
192 understanding of why a person might want or not want to participate.
193

194 Given the variability in the study design, the design details that are presented as key information
195 will also vary. In many cases, key details of the design would include (1) the expected duration
196 of the prospective subject's participation, (2) a high-level description of the major procedures
197 involved, (3) a brief description of any investigational medical product and its marketing
198 authorization status, and (4) identification of any experimental procedures, which for HHS-
199 regulated research could include research procedures outside of a clinical research context (e.g.,
200 educational research).¹⁹ It could be helpful to also include a discussion emphasizing the number
201 of visits and time duration per visit so that prospective subjects understand the total time
202 commitment involved with participating in the study.
203

204 When the key information section presents details about investigational medical products or
205 other investigational interventions, interested parties should consider including information on
206 whether the study design will include a placebo or whether a sham procedure (e.g., a procedure
207 with a non-working device to blind the study design to avoid biasing results) will be used, how
208 subjects will be assigned to a particular regimen (e.g., randomization), and what treatment or
209 intervention options are available following the study (if any). Interested parties should also
210 consider providing information on how an investigational medical product and/or participation in
211 the study is similar to or different from the care the prospective subject would receive if not
212 enrolled in the study.
213

214 3. *Reasonably Foreseeable Risks and Discomforts*²⁰

215
216 The discussion of risks and discomforts is generally among one of the most important and
217 complex required elements of informed consent, and we recommend that this topic be addressed
218 in the key information section. We recommend providing information about the most common
219 and serious risks and discomforts in the key information section to inform a prospective subject's
220 decision about participation.²¹ Key information about risks and discomforts of research
221 participation should be included on the first page of the key information section, if possible. If
222 the key information section does not include all risk-related information, the key information
223 section should note that fact and include a page cross-reference (or hyperlink for electronic
224 documents) that directs prospective subjects to the appropriate section of the consent form where
225 complete information is located.

¹⁹ 21 CFR 50.25(a)(1) and 45 CFR 46.116(b)(1). For FDA-regulated clinical investigations, see the FDA guidance for IRBs, clinical investigators, and sponsors *Informed Consent*.

²⁰ 21 CFR 50.25(a)(2) and 45 CFR 46.116(b)(2).

²¹ See, e.g., the Informed Consent Discussion Tool in Lentz, J, M Kennett, J Perlmutter, and A Forrest, 2016, Paving the Way to a More Effective Informed Consent Process: Recommendations from the Clinical Trials Transformation Initiative, *Contemp Clin Trials*, 49:65–69, p. 67, doi: 10.1016/j.cct.2016.06.005.

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226
227 To help prospective subjects assess risks, interested parties should consider prioritizing key risks
228 from any investigational medical products, research procedures, or other aspects of the study, at
229 the beginning of the information about risks. It may be appropriate in the key information
230 section to present only the most important risks or discomforts based on frequency or magnitude,
231 rather than listing all reasonably foreseeable risks.²² In clinical studies involving investigational
232 medical products, the possibility that the product may present unknown risks to prospective
233 subjects should generally be included as key information. Information about any potential risks
234 should be explained in detail when possible, including, as applicable, the possibility that
235 participation may not improve or could exacerbate a prospective subject's condition.

236
237 We recommend that interested parties clearly delineate between risks and discomforts associated
238 with an investigational medical product or other investigational procedures (e.g., educational or
239 behavioral health interventions) and the risks and discomforts associated with other research
240 interventions or procedures (e.g., additional imaging studies that would not ordinarily be part of
241 clinical care). Also, the degree to which the risks and potential benefits in the study are likely to
242 differ from the risks and benefits of clinical care should be included as key information when
243 appropriate.

244
245 In some cases, the key information section may include actions that will be taken to monitor and
246 mitigate risks, such as planned safety monitoring, dose adjustments, or discontinuation of a
247 subject's participation in the research.

248 249 4. *Reasonably Expected Benefits*²³

250
251 Any reasonably expected benefits of participating in research, either to prospective subjects or
252 others, are likely to be considered key information and could be a major determinant of whether
253 a prospective subject decides to participate in a study. If there is no potential for direct benefit to
254 the prospective subject, this point should be clearly stated. In general, for clinical research, it is
255 important that prospective subjects understand that research is not the same as clinical care and
256 that there may be considerable uncertainty about any potential benefits.²⁴ Details about any
257 potential benefits of participation in a study should be presented in a manner that does not
258 convey an inappropriate or overly optimistic representation of the facts. Potential benefits
259 should be explained in terms of any direct impact to the prospective subject, in addition to the

²² See Office for Human Research Protections, Attachment C – New “Key Information” Informed Consent Requirements: SACHRP Commentary on the New “Key Information” Informed Consent Requirements, October 17, 2018, available at <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-november-13-2018/index.html>. The recommendations in this draft guidance concerning reasonably foreseeable risks in key information are consistent with SACHRP's recommended approaches.

²³ 45 CFR 46.116(b)(3) and proposed 21 CFR 50.25(a)(3), 87 FR 58733 at 58749 (September 28, 2022).

²⁴ The assumption of research subjects that decisions about their care are being made solely with their benefit in mind is termed *therapeutic misconception*. See Appelbaum, PS, LH Roth, and C Lidz, The Therapeutic Misconception: Informed Consent in Psychiatric Research, *International Journal of Law and Psychiatry*, 1982, 5:319–329.

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260 anticipated societal benefit of the research. Any reasonably expected benefits of research
261 participation should also be described in simple and straightforward terms. When appropriate,
262 the description of the potential benefits should include an explanation of any potential impact on
263 a prospective subject's health condition or illness. For example, if a clinical trial is being
264 conducted to assess whether an investigational medical product may reduce tumor size, the key
265 information section should indicate that it is unknown whether the investigational medical
266 product will result in a change in tumor size and that if there is a change, it is not known if that
267 change would affect the prospective subject's quality or length of life.

268
269 When evaluating potential benefits for inclusion in the key information section, we recommend
270 that interested parties consider only those benefits that may result from the research (as
271 distinguished from benefits of therapies or other interventions outside of a research setting (e.g.,
272 some behavioral interventions) that prospective subjects would receive even if not participating
273 in research).

274 275 5. *Appropriate Alternative Procedures*²⁵

276
277 In many circumstances, key information should include a clear and concise description of
278 alternative procedures or courses of treatment, if any, that might be appropriate for the
279 prospective subject. For clinical studies, consider first informing prospective subjects about care
280 they would likely receive if not involved in the study and then providing them with information
281 to help them understand how the care they would receive in the study differs. The emphasis
282 should be on increasing awareness of alternatives because the choice between available
283 alternatives is expected to vary based on individual values and preferences.

284
285 When conveying appropriate alternative procedures or courses of treatment, we recommend
286 providing a description of any reasonably foreseeable risks or discomforts and potential benefits
287 associated with these alternatives. However, a lengthy and detailed description of the risks and
288 benefits of all alternatives may not be appropriate to include in the key information section
289 because such information is likely to vary based on a prospective subject's health condition and
290 past treatment experience as well as the type of study. All of this information need not appear in
291 the key information section but should be included in the remainder of the consent document and
292 as part of the discussion during the consent process.

293 294 6. *Compensation and Medical Treatments for Research-Related Injuries*²⁶

295
296 For research involving more than minimal risk, we recommend addressing as key information
297 details related to any medical treatments and compensation available to prospective subjects if
298 injury occurs as a result of participation. Including this information as part of the key

²⁵ 21 CFR 50.25(a)(4) and 45 CFR 46.116(b)(4).

²⁶ 21 CFR 50.25(a)(6) and 45 CFR 46.116(b)(6).

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299 information may be especially important when there are no plans to compensate prospective
300 subjects for the costs related to the treatment of research-related injuries.²⁷

301

302 7. *Costs Related to Subject Participation*²⁸

303

304 We recommend that interested parties consider whether the key information section should also
305 address costs the prospective subject may incur when participating in a study. If the sponsor or
306 investigator intends to charge for the cost of tests, procedures, products, and/or interventions
307 (including interventions outside of a clinical setting) used during the study, information about
308 costs that may be incurred by a prospective subject or whether the prospective subject's health
309 insurance could be charged (along with information on how to determine whether health
310 insurance will cover costs) should be included in the key information section. The key
311 information section could also inform prospective subjects about whether they will be
312 reimbursed for study-related expenses (e.g., mileage, parking, airfare, lodging, childcare)
313 because such information may influence a prospective subject's decision to participate.
314 Similarly, incentives to encourage participation, as well as payments for a prospective subject's
315 time, inconvenience, and/or discomfort, may be appropriate to include as key information.

316

317 **C. Supplemental Information That Could Be Included Within Key Information**

318

319 While not required, supplemental information beyond the basic and additional consent elements
320 may be included in the key information section when it is likely to be important to the
321 prospective subject's decision about research participation. For example, an investigator
322 conducting a study that could involve risks to others not participating in research (e.g.,
323 radioactive interventions, potential shedding of a virus in gene therapy studies) may want to
324 highlight in the key information section the potential risks to these third parties.

325

326 Identifying information beyond the basic and additional elements of informed consent that an
327 investigator might want to include with the key information can be complex. The Secretary's
328 Advisory Committee on Human Research Protections (SACHRP)²⁹ has provided
329 recommendations on approaches to providing key information consistent with the provision
330 included in the revised Common Rule.³⁰ For example, SACHRP addresses several approaches,
331 including preparing the key information section from a prospective subject's perspective by

²⁷ For ways to address compensation, medical treatments, and information for research-related injuries, see the FDA guidance for IRBs, clinical investigators, and sponsors *Informed Consent*.

²⁸ 21 CFR 50.25(b)(3) and 45 CFR 46.116(c)(3).

²⁹ See footnote 22.

³⁰ *Ibid.* See also 45 CFR 46.116(a)(5)(i).

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332 keeping certain questions about the research in mind. The following list of questions is
333 consistent with, but not limited to, SACHRP’s recommendations:³¹

- 334
- 335 (1) What aspects of research participation or this particular study are likely to be unfamiliar
336 to a prospective subject, to diverge from their expectations, or to require special
337 attention?
- 338 (2) What information about prospective subjects is being collected as part of the research?
- 339 (3) What are the plans to share and protect data that may be of concern to a prospective
340 subject?
- 341 (4) What impact will participating in this research have on a prospective subject outside of
342 the research? For example, will it reduce options for standard treatments, prevent
343 prospective subjects from accessing future care or from participating in other studies, or
344 impact personal activities such as driving or sun exposure?
- 345 (5) How will a prospective subject’s experience in this study differ from treatment outside of
346 the study?
- 347 (6) How is this research novel?
- 348 (7) What investigator’s conflict of interest (if any) may be of interest to prospective subjects?
- 349 (8) How can prospective subjects access any investigational medical products or other
350 interventions examined in the study following completion of the study?

351 The answers to these and similar questions can be used to help identify information that could be
352 appropriate to include with the key information for a given study. We note that this list is not
353 exhaustive and should not be used as a checklist.

354

D. Example of Key Information Section

355

356

357 The appendix to this guidance presents one example of an approach to key information that may
358 be considered by interested parties when developing a key information section and may be
359 considered by IRBs when reviewing consent forms. The language and formatting used are
360 offered as suggestions only, and other language and formatting may be used where appropriate.
361 Depending on the study, it may be appropriate for the key information section to include other
362 informed consent elements from those selected for the example.

363

364

³¹ See appendix I in the Office for Human Research Protections, Attachment C – New “Key Information” Informed Consent Requirements: SACHRP Commentary on the New “Key Information” Informed Consent Requirements, October 17, 2018, available at <https://www.hhs.gov/ohrp/sachrp-committee/recommendations/attachment-c-november-13-2018/index.html>.

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365 **IV. FACILITATING UNDERSTANDING**

366
367 The revised Common Rule at 45 CFR 46.116(a)(5)(ii) requires that “informed consent as a
368 whole must present information in sufficient detail relating to the research and be organized and
369 presented in a way that does not merely provide lists of isolated facts, but rather facilitates the
370 prospective subject’s or legally authorized representative’s understanding of the reasons why one
371 might or might not want to participate.” This provision applies to the consent document as a
372 whole, and the principles are also expected to be applicable to any presentation of consent
373 information (e.g., written, oral, or electronic).³² FDA’s proposed revisions to its regulations at
374 21 CFR 50.20(e)(2) would also include this requirement.³³ Our recommendations on how
375 consent forms can be organized and presented in a way to facilitate understanding are included in
376 the following sections.

377 378 **A. Using Bubbles for the Key Information Section**

379
380 To help present key information in a simple, concise format, we recommend that interested
381 parties consider organizing information within a defined border (e.g., rounded boxes creating a
382 discrete unit of information), referred to here as *bubbles*, or another format that makes the
383 content easy to read and understand. (See the appendix to this guidance for an example of the
384 bubble format for the key information section.) Discrete bubbles addressing separate topics,
385 such as the purpose of the research, potential risks, or alternative therapies, may facilitate a
386 prospective subject’s understanding of the information.³⁴

387
388 Research has explored consumers’ comprehension of alternative versions of prescription drug
389 labeling information to assess whether certain formats improved comprehension.³⁵ The research
390 found that consumers had better comprehension when information was provided in a simple
391 format, with information organized or grouped together within a defined border (e.g., rounded
392 boxes creating a discrete unit of information that can be thought of as a bubble).³⁶

393
394 In addition to using the bubble format or a similar approach for the key information section,
395 other helpful approaches to formatting and organization could be used, including formatting text
396 into two columns, using bullet points to simplify long explanations, and including ample white

³² See the FDA and OHRP joint guidance for IRBs, investigators, and sponsors *Use of Electronic Informed Consent: Questions and Answers*.

³³ Proposed 21 CFR 50.20(e)(2) (87 FR 58733 at 58749, September 28, 2022).

³⁴ See footnote 12.

³⁵ *Ibid.*

³⁶ *Ibid.* (See page 1597 in Boudewyns et al. (footnote 12)). Note that this article compared three formats, including a bubble format in which rounded boxes were aligned in two vertical columns and a format used for over-the-counter (OTC) medications that organized information into boxes that ran the width of the page. A third approach with paragraphs followed the MedGuide format and was used as a control.

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397 space or empty space around discrete bubbles. Such formatting approaches may make
398 documents easier to read.³⁷

399

B. Organization and Presentation of the Entire Consent Form

401

402 The revised Common Rule at 45 CFR 46.116(a)(5)(ii) requires, and 21 CFR 50.20(e)(2) of
403 FDA’s proposed rule would also require, that consent information be presented in a way that
404 facilitates the understanding of prospective subjects, and, like the key information provision,
405 could also be addressed in multiple ways. We recommend following plain language principles
406 for the entire consent form.³⁸ Plain language principles generally involve a combination of text-
407 based and visual approaches (e.g., pictures and diagrams), including organizing information with
408 the most important points first, breaking complex information into understandable groups, using
409 simple language, and defining technical terms.³⁹ The use of bubbles beyond the key information
410 section may not be feasible. However, we suggest that interested parties consider using other
411 formatting suggestions discussed in section IV.A of this guidance (e.g., bulleted lists, two-
412 column format, white space), as appropriate, for the entire consent form.

413

1. Providing Content in Sufficient Detail

414

415
416 The revised Common Rule at 45 CFR 46.116(a)(5)(ii) requires, and 21 CFR 50.20(e)(2) of
417 FDA’s proposed rule would also require, that the consent “present information in sufficient detail
418 relating to the research.” This provision applies to information that is required to be included in
419 informed consent. Sufficient detail about research information may be contained within a key
420 information section or elsewhere in the consent form, depending on where it is most appropriate.

421

2. Organization

422

423
424 The revised Common Rule at 45 CFR 46.116(a)(5)(ii) requires that informed consent as a whole
425 “be organized and presented in a way that does not merely provide lists of isolated facts, but
426 rather facilitates the prospective subject’s or legally authorized representative’s understanding of
427 the reasons why one might or might not want to participate.” FDA’s proposed rule, if finalized
428 as proposed, would include identical language in 21 CFR 50.20(e)(2).

429

430 Thoughtful organization of consent documents can help prospective subjects better understand
431 the information presented in the entire consent form. One suggestion would be to use a tiered
432 approach, particularly for more-complex study designs.⁴⁰ The first tier would provide the key

³⁷ Ibid.

³⁸ See Hadden, KB, LY Prince, TD Moore, LP James, JR Holland, and CR Trudeau, 2017, Improving Readability of Informed Consents for Research at an Academic Medical Institution, *J Clin Trans Sci*, 361–365, doi: 10.1017/cts.2017.312. Also see footnote 21.

³⁹ See footnote 12.

⁴⁰ See footnote 21.

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433 information. The second tier could be divided into different topics with the remaining consent
434 elements (or with further details of consent elements partially addressed in the key information
435 section). A third tier could address other information that is not required by the regulations or
436 could provide details of required elements, such as a detailed description of the study design, a
437 schedule of procedures at each visit, and language about how confidential information may be
438 handled. If appropriate for the consent form, the third tier also could include glossaries and
439 references. We recommend including a table of contents and page numbers (or hyperlinks for
440 electronic documents) to cross-reference related topics.

441

442 3. *Understandable Language*

443

444 Information should be presented in plain language and at a level prospective subjects would
445 likely comprehend; explanations should be included for scientific and medical terms.⁴¹ An
446 assessment of the needs and characteristics of the prospective subject population, including their
447 age, any relevant medical diagnosis, level of English proficiency, education level, and cognitive
448 abilities, can be helpful in developing consent information that facilitates understanding.
449 Information should be provided in the primary language of a prospective subject with limited
450 English proficiency.⁴² Although not required, one possible way to evaluate whether the
451 information is presented in a way that facilitates understanding is to have the information
452 reviewed by individuals unfamiliar with the research. This may be particularly helpful for forms
453 translated into additional languages. For example, this could include review by patient advocacy
454 groups or a sample of individuals from the subject population.

⁴¹ See Jefford, M, and R Moore, 2008, Improvement of Informed Consent and the Quality of the Consent Form, *Lancet Oncol*, 9(5):485–493; p. 489. Also see footnote 38 and footnote 21.

⁴² FDA and OHRP strongly encourage stakeholders to ensure that informed consent documents are accessible to individuals with limited English proficiency. To the extent an organization receives Federal financial assistance from HHS, the organization must comply with Title VI of the Civil Rights Act of 1964 and its implementing regulations. This guidance provides information to assist IRBs, investigators, and sponsors in complying with OHRP’s regulation and FDA’s proposed regulation, if and when it is finalized, related to the key information section of informed consent. This document does not provide guidance on how to comply with any regulatory obligations stemming from a source outside of the statutes FDA and OHRP administer and their respective regulations.

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455 **APPENDIX: A HYPOTHETICAL CLINICAL TRIAL**

456
457 **Title:** A trial to evaluate the use of product X to treat health condition Y
458
459

460 **Key Information You Should Know Before Agreeing to Participate**

461
462 The key information that follows can help you learn more about this clinical trial. It can also help you decide
463 whether or not to take part in the trial. **Please read the entire consent form or have someone read it with**
464 **you.** If there is anything that you do not understand, please talk to the trial doctor or team to have your
465 questions answered before signing the consent form.
466

467
468
469 **Voluntary Participation and Right to Discontinue Participation**

470
471 We are asking you to consent to participate in this research study. Your participation is voluntary and should
472 be based on what is important to you. It is your choice to participate in this trial. If you agree to participate,
473 you may leave at any time without penalty or loss of benefits to which you are otherwise entitled.
474

475
476 **Purpose of the Research**

477
478 The purpose of the trial is to find out if product X, the product that is being studied, is safe and effective in
479 treating adults like you who have health condition Y.
480

481
482
483 **Key Reasonably Foreseeable Risks and Discomforts (see page #)**

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

486 **Reasonably Expected Benefits (see page #)**

- 487 • Prior research suggests product X may
488 improve condition Y.
- 489 • Researchers are studying product X in
490 this trial to learn more about whether
491 product X will improve condition Y.
- 492 • If you are randomly assigned to take
493 product X, product X may improve your
494 health condition Y. If you are randomly
495 assigned to take the inactive pill, you will
496 not receive product X and will not benefit
497 directly.
- 498 • By participating in this trial, you will help
499 researchers learn how product X may help
500 people with condition Y.

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Expected Duration and Procedures to Be Followed (see pages #)

- To learn if product X makes a difference, it is important for the trial to include people who will get a placebo (inactive pill). With this information, researchers can compare the effects of product X or the placebo on your health condition.
- A computer will assign you randomly, like flipping a coin, to a group taking product X or to a group taking the inactive pill.
- You and your doctors cannot choose which group you will be assigned to.
- This trial will take 6 months and require weekly clinic visits (24 visits total), with each visit expected to take 1 hour. At each visit, you will have blood drawn and a procedure to test your blood oxygen content.

Appropriate Alternative Procedures (see page #)

- In this trial, if you are assigned to take the placebo, you cannot take product X.
- Before joining the trial, you should talk to your doctor about alternative approved treatment options for your condition, and whether or not this trial is a good choice for you.
- Before agreeing to join, you should review information in the rest of the consent form.

Compensation and Medical Treatments for Research-Related Injuries (see page #)

- If you experience an injury caused by your participation in this research, the medical treatment of your injury will be paid for.
- More information on medical treatments for research-related injuries is available in the consent form.

Costs Related to Subject Participation (see page #)

- You may incur costs by participating in this trial.
- The sponsor will reimburse you for any travel costs for mileage, parking, and other expenses.
- In addition, the sponsor will pay you for your time participating in the trial.

Additional Information (see page #)

- If trials show that product X is effective in treating your health condition, you may be able to continue to take product X in a related trial.