Notice of Proposed Rulemaking

Questions posed within the new rule for public comment:

Section I.

**Topic: Guiding Principles for Proposed Changes**

1. Public comment is sought on whether the proposed changes will achieve the objectives of (i) decreasing administrative burden, delay and ambiguity for investigators, institutions, and IRBs, and (ii) strengthening, modernizing, and making the regulations more effective in protecting research subjects. (the proposed changes as a whole)

Section II.

**Topic: Scope and Applicability of the Regulations; Expanding the Definition of “Human Subject to Cover Research with Non-identified Biospecimens**

2. Would providing a definition of biospecimen be helpful in implementing this provision? If so, how might the definition draw a line between when a biospecimen is covered by the Common Rule, and when processing of biological materials (e.g., to create a commercial product used for treatment purposes) has sufficiently altered the materials so that they should not be subject to the regulations? Would only covering biospecimens that include nucleic acids draw an appropriate line? (Section II.A.1.a-e; pages 46-63)

3. To what extent do the issues raised in this discussion suggest the need to be clearer and more direct about the definition of identifiable private information? How useful and appropriate is the current modifier “may be readily ascertained” in the context of modern genomic technology, widespread data sharing, and high speed computing? One alternative is to replace the term “identifiable private information” with the term used across the Federal Government: personally identifiable information (PII). The Office of Management and Budget’s concept of PII refers to information that can be used to distinguish or trace an individual's identity (such as their name, social security number, biometric records, etc.) alone, or when combined with other personal or identifying information which is linked or linkable to a specific individual, such as date and place of birth, mother’s maiden name, etc. It is acknowledged that replacing “identifiable private information” with “PII” would increase the scope of what is subject to the Common Rule. However, the practical implications of such an expansion, other than the need to ensure that the data are securely stored and otherwise protected against disclosure, may be minimal. Public comment is requested on the advantages and disadvantages of such a change. (Section II.A.1.a-e; pages 46-63)

4. Which of the three proposals regarding the definition of human subject achieves the most reasonable tradeoff between the principles of autonomy (including transparency and level of trust) versus beneficence (as measured by facilitating valuable research)? (Section II.A.1.a-e; pages 46-63)

5. Public comment is sought regarding any concerns that you have about each of the three proposals, including concerns about implementation or burden to investigators and institutions. (Section II. A.1.a-e; pages 46-63)
**Topic: Explicit Exclusion of Activities from the Common Rule: Program Improvement**

6. Public comment is sought for whether this excluded activity should simply be discussed in the text of the final rule’s preamble, and guidance produced to assist investigators in making such a determination, or whether any other similar exclusions should be addressed. (Section II.A.2.a.i.; pages 65-70)

7. Public comment is sought for whether biospecimens should not be included in any of these exclusion categories, and if so, which ones. (Section II.A.2.a.i; pages 65-70)

**Topic: Explicit Exclusion of Activities from the Common Rule: Oral History, Journalism, Biography, and Historical Scholarship Activities; Criminal Justice Activities; Quality Assurance and Quality Improvement Activities; Public Health Surveillance; Intelligence Surveillance Activities**

8. Public comment is requested on whether the parameters of the exclusions are sufficiently clear to provide the necessary operational guidance, or whether any additional criteria or parameters should be applied to clarify or narrow any of these exclusions. (Section II.A.2.a.ii-v; pages 71-80)

**Topic: Explicit Exclusion of Activities from the Common Rule: Low risk and Already Subject to Independent Controls (no request for comment)**

**Topic: Explicit Exclusion of Activities from the Common Rule: Educational Tests, Survey Procedures, Interview Procedures, or Observation of Public Behavior**

9. Public comment is requested on the extent to which covering any of these activities under the Common Rule would substantially add to the protections provided to human research subjects. (Section II.A.2.b.iii; pages 84-89)

10. Public comment is sought on whether this exclusion should only apply to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement. If so, please comment on what kind of information should be included in the notice such as the research purpose, privacy safeguards, contact information, ability to optout, etc. Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence? (Section II.A.2.b.iii; pages 84-89)

11. Public comment is sought regarding whether it is reasonable to rely on investigators to make self-determinations for the types of research activities covered in this particular exclusion category. If so, should documentation of any kind be generated and retained? (Section II.A.2.b.iii pages 84-89)

12. Public comment is sought regarding whether some or all of these activities should be exemptions rather than exclusions. (Section II.A.2.b.iii pages 84-89)

13. Public comment is sought regarding whether these exclusions should be narrowed such that studies with the potential for psychological risk are not included. Are there certain topic areas of sensitive information that should not be covered by this exclusion? If so, please provide exemplary language to characterize such topic areas in a manner that would provide clarity for implementing the Rule. (Section II.A.2.b.iii; pages 84-89)

14. For activities captured under the third element of this exclusion, do the statutory, regulatory, and other policy requirements cited provide enough oversight and protection that being subject to expedited
review under the Common Rule would produce minimal additional subject protections? If so, should the exclusion be broadened to also cover secondary analysis of information collected pursuant to such activities? (II.A.2.b.iii; page 84-89)

15. Public comment is requested on the extent to which excluding any of these research activities from the Common Rule could result an actual or perceived reduction or alteration of existing rights or protections provided to human research subjects. Are there any risks to scientific integrity or public trust that may result from excluding these research activities from the Common Rule? (Section II.A.2.b.iii; pages 84-89)

**Topic: Explicit Exclusion of Activities from the Common Rule: Collection or Study of Information That Has Been or Will Be Collected**

16. Public comment is sought regarding whether it is reasonable to rely on investigators to make self-determinations for the types of research activities covered in this particular exclusion category. If so, should documentation of any kind be generated and retained? (Section II.A.2.b.iv; pages 91-93)

17. Public comment is requested on the extent to which covering any of these activities under the Common Rule would substantially add to the protections provided to human research subjects. Is there a way in which this exclusion should be narrowed? Public comment is also sought regarding whether activities described here should appear as an exclusion or as an exemption. (Section II.A.2.b.iv; pages 91-93)

**Topic: Explicit Exclusion of Activities from the Common Rule: Research Conducted by a Government Agency Using Government-Generated or Government-Collected Data**

18. Public comment is sought on whether this or a separate exclusion should also include research involving information collected for non-research purposes by non-federal entities where there are comparable privacy safeguards established by state laws and regulations, or whether such non-federally conducted research would be covered by the proposed exemption at §__.104(e)(2). (Section II.A.2.b.v; pages 93-95)

19. Public comment is requested on the extent to which covering any of these activities under the Common Rule would substantially add to the protections provided to human research subjects. (Section II.A.2.b.v; pages 93-95)

20. Public comment is sought regarding whether it is reasonable to rely on investigators to make self-determinations for the types of research activities covered in this particular exclusion category. If so, should documentation of any kind be generated and retained? (Section II.A.2.b.v; pages 93-95)

21. Public comment is sought regarding whether some or all of these activities should be exemptions rather than exclusions. (Section II.A.2.b.v; pages 93-95)

**Topic: Explicit Exclusion of Activities from the Common Rule: Activities Covered by HIPAA**

22. Public comment is requested on whether the protections provided by the HIPAA Rules for identifiable health information used for health care operations, public health activities, and research activities are sufficient to protect human subjects involved in such activities, and whether the current process of
seeking IRB approval meaningfully adds to the protection of human subjects involved in such research studies. (Section II.A.2.b.vi; pages 95-97)

23. Public comment is sought regarding to what extent the HIPAA Rules and HITECH adequately address the beneficence, autonomy, and justice aspects for the collection of new information (versus information collected or generated in the course of clinical practice, e.g., examination, treatment, and prevention). Should this exclusion be limited to data collected or generated in the course of clinical practice? If additional data collection is allowable, should it be limited to what is on the proposed Secretary’s list of minimal risk activities (discussed in more detail below in II.F.2 of this preamble)? (Section II.A.2.b.vi; pages 95-97)

24. Public comment is requested on whether additional or fewer activities regulated under the HIPAA Privacy Rule should be included in this exclusion. (Section II.A.2.b.vi; pages 95-97)

**Topic: Applicability of Exclusions to Subparts i.e., Subpart B Pregnant Women, Fetuses, and Neonates; Subpart C Prisoners; Subpart D Children**

25. Should research involving prisoners be allowed to use any or all of the exclusions found at §__.101(b)(2) and (3), as currently proposed? (Section II.A.2.c; pages 98-100)

26. Are there certain provisions within the broader categories proposed at §__.101(b)(2) and (3) to which the subparts should or should not apply? (Section II.A.2.c; pages 98-100)

**Topic: Proposed Exemptions; Making Exempt Research Determinations**

27. Public comment is sought regarding how likely it would be that institutions would allow an investigator to independently make an exempt determination for his or her own research without additional review by an individual who is not involved in the research and immersed in human research protection e.g., a member of the IRB Staff. (Section II.A.3.a; pages 100-109)

28. Public comment is sought regarding whether an investigator would be able to contrive his or her responses to the automated exemption decision tool in order to receive a desired result i.e., an exempt determination, even if it does not accurately reflect the research activities. (Section II.A.3.a; pages 100-109)

29. Public comment is sought on whether it would be more appropriate for some of the exempt categories than others to rely on the exemption determination produced by the decision tool where investigators themselves input the data into the tool, or whether there should be further administrative review in such circumstances. (Section II.A.3.a; pages 100-109)

30. Public comment is sought regarding whether relying on the exemption determination produced by the decision tool where investigators themselves input the data into the tool as proposed would reduce public trust in research. (Section II.A.3.a; pages 100-109)

31. Public comment is sought regarding how likely it would be that institutions would rely on such a decision tool to provide a safe harbor for an investigator making a determination that the proposed research qualifies for an exemption, or whether developing such a tool would not be worthwhile, and whether institutions would be able to adequately manage exemption determinations without the use of the decision tool. (Section II.A.3.a; pages 100-109)
32. Public comment is sought regarding what additional information should be required to be kept as a record other than the information submitted into the decision tool, for example, a study abstract, the privacy safeguards to be employed, or any notice or consent document that will be provided. (Section II.A.3.a; pages 100-109)

33. Public comment is sought regarding the value of adding an auditing requirement. (Section II.A.3.a; pages 100-109)

**Topic: Exemptions Subject to the Documentation Requirements of §__.104(c) and No Other Section of the Proposed Rule Research Conducted in Established or Commonly Accepted Educational Settings**

34. Public comment is sought on whether this exemption category should only apply to research activities in which notice that the information collected will be used for research purposes is given to prospective subjects or their legally authorized representatives as a regulatory requirement, when not already required under the Privacy Act of 1974. If so, comment is sought on what kind of information should be included in the notice, such as the research purpose, privacy safeguards, contact information, etc. Comment is also sought on how such a notice should be delivered, e.g., publication in a newspaper or posting in a public place such as the school where the research is taking place, or by individual email or postal delivery. Note that other requirements, such as those of the Family Educational Rights and Privacy Act (FERPA) or the Protection of Pupil Rights Amendment, may also apply. Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence? (Section II.A.3.b.i; pages 111-113)

35. Public comment is sought on whether the privacy safeguards of §__.105 should apply to the research included in §__.104(d)(1), given that such research may involve risk of disclosure of identifiable private information. (Section II.A.3.b.i; pages 111-113)

**Topic: Research and Demonstration Projects Conducted or Supported by a Federal Department or Agency**

36. Public comment is sought on whether this exemption category should only apply to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement. If so, comment is sought on what kind of information should be included in the notice, e.g., the research purpose, privacy safeguards, or contact information. Also comment on how such a notice should be delivered; e.g., publication in a newspaper or posting in a public place, or by individual email or postal delivery. Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence? In many cases, it may be that individual notice or consent to all potentially affected persons before the research or demonstration commences is ordinarily impossible in the conduct of such studies. For example, if a research or demonstration project will affect all inhabitants of a large geographic area (e.g., a housing, a police patrol, a traffic control, or emergency response experiment), or all clients or employees of a particular program or organization or setting will be subject to a new procedure being tested (e.g. a new approach to improving student performance, a new anti-smoking or anti-obesity program, a new method for evaluating employee performance), would it be possible to make participation voluntary for all affected individuals, or even to identify and inform all affected individuals in advance? (Section II.A.3.b.ii; pages 114-120)
37. Public comment is sought on whether this exemption category is appropriate based on the recognition that alternative processes are in place in which ethical issues raised by research in public benefit or service programs would be addressed by the officials who are familiar with the programs and responsible for their successful operation under state and federal laws, rather than meeting specific risk-based criteria, or whether risk limitations should be included, and if so, what those limitations should be. Though long-standing, this exemption has never identified specific risk-based criteria, or risk limitations to bound the type of projects that may be covered. When originally promulgated, the exemption did stipulate that following the review of such projects, if the Secretary determines that the research or demonstration project presents a danger to the physical, mental, or emotional well-being of a participant or subject, then written informed consent would be required. Public comment is sought on whether to limit the risk that can be imposed on subjects while using this exemption, and if so, how to characterize those limits in a clear fashion. If more than minimal risk interventions are included, public comment is sought on whether, for transparency, this should be made clear in the regulatory text.

With regard to the issue of risks encountered by participants in such research or demonstration projects, comments are also sought regarding the argument that any and every demonstration project involving changes in public benefit or service programs (e.g., water or sewage treatment programs or pollution control programs, programs involving educational procedures, or programs involving emergency procedures related to extreme weather events, etc.) exposes those affected to possible risks of some kind. In this regard, those risks are ordinarily and perhaps always no different in kind or magnitude than those involved in simply making the change in procedures without using research tools to evaluate them. For example, health care providers could be required to perform certain sanitation reforms to prevent patient infections whether or not such reforms were first tested in practice through a research or demonstration project. It is common for all Federal departments and agencies that regulate private or public organizations to impose conditions of participation in public programs providing for safety, program integrity, financial reporting, etc. Public comment is sought regarding whether there should be conditions (e.g., an individual notice or consent requirement) imposed on such research or demonstration projects involving public benefit or service programs which might lead to significant impediments or limitations on testing and evaluation before or after being imposed program wide. Would the effect of imposing expensive or impracticable conditions on public benefits or services evaluations be to reduce the number of such evaluations and consequently to expose program participants to increased risk through exposure to untested reforms? (Section II.A.3.b.ii; pages 114-120)

38. Public comment is sought on whether the existing privacy safeguards for such activities including the Privacy Act, HIPAA rules, and other federal or state privacy safeguards provide sufficient independent controls, or whether other safeguards such as the privacy safeguards of §__.105 should be applied. (Section II.A.3.b.ii; pages 114-120)

**Topic: Research Involving Benign Interventions in Conjunction with the Collection of Data from an Adult Subject**

39. Public comment is sought on whether this exemption category should only apply to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement. If so, comment is sought on what kind of information should be included in the notice, such as the research purpose (if authorized deception is not utilized), privacy safeguards, contact information, etc. Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence? (Section II.A.3.b.iii; pages 123-127)
40. Public comment is sought regarding what improvements could be made to the language describing the type of interventions in this exemption category so as to make clear what interventions would or would not satisfy this exemption category. (Section II.A.3.b.iii; pages 123-127)

41. Public comment is sought on whether it is reasonable, for purposes of this exemption, to rely on the exemption determination produced by the decision tool where investigators themselves input the data into the tool, or whether there should be further administrative review in such circumstances. (Section II.A.3.b.iii; pages 123-127)

**Topic: Taste and Food Quality Evaluation and Consumer Acceptance Studies**

42. Public comment is sought on whether this exemption category should be narrowed to apply only to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement. If so, comment is sought on what kind of information should be included in the notice such as the research purpose, privacy safeguards, contact information, etc. Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence? Should prospective subjects be given the explicit opportunity to opt out of such research? (Section II.A.3.b.iv; pages 127-128)

**Topic: Exemptions Subject to the Documentation Requirements and the Privacy Safeguards**

43. Public comment is sought on the concept of requiring such minimum safeguards and limitations on disclosure, as well as whether the requirements of the proposed §__.105 would constitute a broadening of IRB responsibilities rather than a streamlining of the implementation of responsibilities that many IRBs already adopted. If an institution does view this as an inordinate broadening of responsibilities, does the institution currently have in place alternative mechanisms for ensuring data security and participant privacy in a research context? Suggestions for alternative approaches to meeting public expectation that federally sponsored research safeguard their data and protect privacy are sought during this public comment period. (Section II.A.3.c.i; pages 129-131)

44. Public comment is sought regarding whether the proposed Rule’s information security requirements for biological specimens and identifiable private information are highly technical and require a level of expertise not currently available to most IRBs. Do these security requirements unrealistically expand IRB responsibilities beyond current competencies? (Section II.A.3.c.i; pages 129-131)

**Topic: Research Involving Educational Tests, Surveys, Interviews, or Observation of Public Behavior if the Information is Recorded with Identifiers and even if the Information is Sensitive**

45. Public comment is sought on whether the proposed exemption regarding the use of educational tests, survey procedures, interview procedures, or observation of public behavior (§__.104(e)(1)) should be applied to research involving the use of educational tests with children and whether it should also be applied to research involving the use of survey or interview procedures with children. If so, for research involving children, should the permissible survey or interview topics be limited in some way? (Section II.A.3.c.ii; pages 132-136)

46. Public comment is sought on whether this exemption category should only apply to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement. If so, comment is sought on what kind of information should be included in the notice such
as the research purpose, privacy safeguards, contact information, etc. Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence? Should prospective subjects be given the explicit opportunity to opt out of such research? (Section II.A.3.c.ii; pages 132-136)

47. Public comment is sought on whether it is reasonable, for purposes of this exemption, to rely on the exemption determinations produced by the decision tool where investigators themselves input the data into the tool, or whether there should be further administrative review in such circumstances? (Section II.A.3.c.ii; pages 132-136)

48. Public comment is sought on whether this exemption category should be narrowed such that studies with the potential for psychological risk are not included. Are there certain topic areas of sensitive information that should not be covered by this exemption? If so, please provide exemplary language to characterize such topic areas in a manner that would provide clarity for implementing the Rule. (Section II.A.3.c.ii; pages 132-136)

**Topic: Secondary Research Use of Identifiable Private Information**

49. Public comment is sought on the types of research that should fall under the proposed exemption. Should the proposed exemption be available to all types of research using identifiable data collected for non-research purposes or should the exemption be available only to a more limited subset of research? For example, should the proposed exemption apply only for research using records and information already subject to comprehensive privacy and other protections in other Federal laws (e.g., records held by the Federal Government subject to the Federal Privacy Act, or records governed by HIPAA or FERPA)? (Section II.A.3.c.iii; pages 137-143)

Depending upon the scope of the exemption, the relationship between this exemption and the exemption proposed at §__.104(f)(2) would need to be clarified. Since a major justification for including this exemption is to reduce burden on IRBs, should the proposed exemption apply only to research for which IRBs typically waive informed consent, that is, where the research could not practicably be carried out without a waiver of informed consent, and the rights and welfare of subjects will not be adversely affected by the waiver? Finally, is there a sufficient need for this exemption at all given the other proposed exclusions and exemptions? (Section II.A.3.c.iii; pages 137-143)

50. Public comment is sought regarding whether the proposed exemption should be limited to research in which individuals had been informed of the potential future research use of their information, and given the opportunity to opt out of having their identifiable private information used for research. If the proposed exemption should be limited in this way, what information should be included in the opportunity to opt out? If the opportunity to opt out is made a condition of the exemption category how should it be structured (e.g., how long and under what circumstances should it remain in effect) and what, if any, impact should the opt out have on other provisions of the rule, such as the ability of an IRB to waive informed consent for a subsequent research study using the individual’s information? Are there other or alternative mechanisms that should be required to respect individuals’ autonomy and other interests? (Section II.A.3.c.iii; pages 137-143)

51. Public comment is sought regarding what should constitute notice for purposes of this exemption category. Given the many different types of data that would be covered by this provision (e.g., data from private entities used for social or behavioral science research, government records for which laws already establish standards for notice, and data publicly available for harvesting from the internet), would it be possible to develop a uniform “notice” requirement? What type of notice, in terms of its
dissemination and scope, should be considered to meet this requirement of the proposed exemption? With regard to the dissemination of the notice, should the notice requirement be permitted to be fulfilled through a general public notice, not specifically directed to individuals who are potential research subjects, such as the notice allowable under the Privacy Act? Would a prominent notice posted in all clinics or other relevant public places where information will be collected be acceptable? Should each individual whose data could be used receive their own notice, such as is required of direct treatment providers covered by the HIPAA Privacy Rule? With regard to the content of the notice required by this proposed exemption, what kind of information should be included in the notice, such as the types of research that might be conducted, privacy safeguards, contact information, etc.? (Section II.A.3.c.iii; pages 137-143)

52. Public comment is sought on whether, on the other hand, prior notice is necessary. Is the notice requirement proposed for this exemption a meaningful and important measure to respect individual autonomy, particularly if the notice requirement could be fulfilled through a general public posting? Current practices suggest that IRBs will frequently waive informed consent for studies involving the secondary use of identifiable private information collected for non-research purposes. If the exemption were to exclude the notice requirement, but continue to require application of the data security and privacy safeguards of §__.105 and restrict the use of identifiable private information to only purposes of the specific research for which the investigator obtained the information, would the exemption better strike a reasonable balance between respect for persons and beneficence, while eliminating the current requirement for IRB review? (Section II.A.3.c.iii; pages 137-143)

53. Public comment is sought as to whether this exemption would provide appropriate protections for research conducted by clinical data registries, while enabling these research activities to proceed without delay, and what should be included in guidance regarding such activities. Public comment is sought regarding the extent to which other exclusions or exemption categories would apply to research conducted by clinical data registries, such that the conditions of this exemption category would not apply. (Section II.A.3.c.iii; pages 137-143)

**Topic: Exemptions Subject to the Documentation Requirements of the Privacy Safeguards, Limited IRB Review and Broad Consent; Exemption for the Storage or Maintenance of Biospecimens or Identifiable Private Information for Secondary Research Use; Exemption for Secondary Research use of Biospecimens or Identifiable Private Information where Broad Consent has been Sought and Obtained**

54. Public comment is sought on whether the NPRM’s proposal of exemption §__.104(f)(2) is the best option, or whether there is a better way to balance respect for persons with facilitating research. Section II.A.3.d; pages 146-157)

55. Public comment is sought on whether and how the provision regarding the return of research results in the proposed exemption §__.104(f)(2) should be revised. Section II.A.3.d; pages 146-157)

56. Public comment is sought on whether there should be an additional exemption that would permit the collection of biospecimens through minimally invasive procedures (e.g., cheek swab, saliva). (Section II.A.3.d; pages 146-157)

**Topic: Applicability of Exemptions to the Subparts i.e., Subpart B Pregnant Woman, Fetuses and Neonates, Subpart C Prisoners, and Subpart D Children**
57. Public comment is sought on whether research involving prisoners should be permitted to apply any or all of the exemption categories found at proposed §__.104, either if the research consists mostly of non-prisoners and only incidentally includes some number of prisoners, as proposed in the NPRM, or if the research intends to involve prisoners as research subjects. (Section II.A.3.e; pages 158-160)

58. Would it be preferable for language at §__.104(b)(2) to resemble the 2002 epidemiologic waiver criteria and state that the exemptions apply except for research where prisoners are a particular focus of the research? (Section II.A.3.e; pages 158-160)

59. Is the proposed application of the exemptions to subparts B and D appropriate? (Section II.A.3.e; pages 158-160)

**Topic: Proposed Changes to Obtaining, Waiving, and Documenting Informed Consent; Required elements of informed consent;**

60. What topics should be addressed in future guidance on improving the understandability of informed consent? (Section II.B.1; pages 162-174)

**Topic: Broad Consent to the Storage, Maintenance and Secondary Research Use of Biospecimens and Identifiable Private Information**

61. Public comment is sought on whether broad consent to secondary research use of information and biospecimens collected for non-research purposes should be permissible without a boundary, or whether there should be a time limitation or some other type of limitation on information and biospecimens collected in the future that could be included in the broad consent as proposed in the NPRM. If a time limit should be required, is the NPRM proposal of up to 10 years a reasonable limitation? Would a limitation related to an identified clinical encounter better inform individuals of the clinical information and biospecimens that would be covered by a broad consent document? (Section II.B.2; pages 175-186)

62. Public comment is sought on whether all of the elements of consent proposed at §__.116(c) should be required for the secondary use of biospecimens or identifiable private information originally collected as part of a research study that was conducted without consent because either the original research study met an exclusion or exempt category of research, or a waiver of consent was approved by an IRB. (Section II.B.1; pages 175-186)

63. Public comment is sought on whether oral consent should be permissible in limited circumstances as proposed under exemption §__.104(f)(1). (Section II.B.2; pages 175-186)

64. Would research subjects continue to be appropriately protected if the definition of “legally authorized representative” were broadened to include individuals authorized by accepted common practice to consent on behalf of another individual to participation in clinical procedures? If the definition of “legally authorized representative” was broadened in this way, public comment is sought on the interpretation of “accepted” and “common” as these terms would be used in the revised definition. (Section II.B.2; pages 175-186)

**Topic: Waiver of Informed Consent or Documentation of Informed Consent**

65. Public comment is sought on how the waiver criterion regarding “practicably” at §__.116(d)(3) could be explicitly defined or otherwise clarified (e.g., what term should replace “practicably”?). (Section II.B.3; pages 186-199)
66. Public comment is sought on the proposed differences between the criteria for waiving informed consent for the research use of biospecimens versus identifiable information. (Section II.B.3; pages 186-199)

67. Public comment is sought on whether the proposal to permit an IRB to waive consent for research involving the use of biospecimens should be included in the regulations. (Section II.B.3; pages 186-199)

68. Public comment is sought on the proposal to permit an IRB to waive consent for the secondary use of biospecimens or information originally collected for research purposes, even if the original research study required subjects’ informed consent. (Section II.B.3; pages 186-199)

69. Public comment is sought regarding how likely investigators are to seek broad consent for the use of identifiable private information (as contrasted with biospecimens), given that there are provisions within the NPRM that would make it easier to do such research without consent (such as the new exemption at §__.104(e)(2)). In this regard, note that the NPRM proposal to prohibit waiver of consent by an IRB if a person has been asked for broad consent and refused to provide it might create a disincentive on the part of investigators from choosing to seek broad consent for research involving secondary use of identifiable private information. Given the costs and time and effort involved in implementing the system for obtaining broad consent for the use of identifiable private information and tracking when people provide consent or refuse to do so, are the benefits to the system likely to outweigh the costs, and if so, should the broad consent provisions be limited to obtaining broad consent for research use of biospecimens? (Section II.B.3; pages 186-199)

70. Public comment is sought on the proposed prohibition on waiving consent when an individual has been asked to provide broad consent under §__.116(c) and refused. In particular, how would this prohibition on waiving consent affect the secondary research use of identifiable private information? If an individual was asked to provide such consent, should the absence of a signed secondary use consent be considered a refusal? Does this prohibition on waiving consent for the secondary use of identifiable private information create a disincentive for institutions to seek broad secondary use consent and instead seek a waiver of consent from an IRB? Under what circumstances, if any, would it be justified to permit an IRB to waive consent even if an individual declined or refused to consent? (Section II.B.3; pages 186-199)

**Topic: Posting of Consent Forms** (Section II.B.4; pages 201-202) No request for comment.

**Topic: Proposed Changes to Protect Information and Biospecimens** (Section II.C; pages 202-213)

**No # pg 208** For the purposes of informing the development of the §__.105 privacy safeguards, comment is sought on what types of safeguards would be appropriate.

**No # og 209** Public comment is sought on whether any of the above referenced statutes or acts would serve the goals of §__.105. Note that the statutes and acts referenced in §__.105(b) are currently referenced in the proposed exclusions at §__.101(b)(2)(i) (exclusion for surveys, educational tests, and public observation) and §__.101(b)(2)(iii) (exclusion for federal departments or agencies to use pre-existing federally generated non-research data). To that end, public comment is also sought as to whether the goals of the NPRM are served by referencing any of the aforementioned statutes, acts, or standards in the exclusions proposed in §__.101(b)(2)(i) and (iii).
71. Public comment is sought regarding whether particular information security measures should be required for certain types of information or research activities and, if so, what measures and for what types of information or research. Specifically, should the safeguards be calibrated to the sensitivity of the information to be collected? (Section II.C; pages 202-213)

72. Are the proposed limitations on re-disclosure more or less restrictive than necessary? Are there additional purposes for which re-disclosure of biospecimens or identifiable private information should be permitted? (Section II.C; pages 202-213)

**Topic: Harmonization of Agency Guidance**

73. Will the proposed language at §__.101(j) be effective in achieving greater harmonization of agency guidance, and if not, how should it be modified? (Section II.D; pages 213-217)

**Topic: Cooperative Research and Proposal to Cover Unaffiliated IRBs Not Operated by an Institution Holding a Federalwide Assurance**

74. Is mandated single IRB review for all cooperative research a realistic option at this time? Please provide information about the likely costs and benefits to institutions. Will additional resources be necessary to meet this requirement in the short term? Should savings be anticipated in the long run? (Section II.E; pages 218-229)

75. What areas of guidance would be needed for institutions to comply with this requirement? Is there something that OHRP could do to address concerns about institutional liability, such as the development of model written agreements? (Section II.E; pages 218-229)

76. Would it be useful for this requirement to include criteria that Federal departments or agencies would need to apply in determining whether to make exceptions to the use of a single IRB requirement? If so, what should these criteria be? (Section II.E; pages 218-229)

77. Are the exceptions proposed appropriate and sufficient, or should there be additional exceptions to this mandate for single IRB review than those proposed in the NPRM? If additional exceptions should be included, please provide a justification for each additional exception recommended. (Section II.E; pages 218-229)

78. Is three years appropriate timing to establish compliance with this provision? (Section II.E; pages 218-229)

**Topic: Changes to Promote Effectiveness and Efficiency in IRB Operations** (Section II.F.1; pages 230-234) No request for comment.

**Topic: Expedited Review Procedures and the Definition of “Minimal Risk”**

79. How often should the Secretary’s list of minimal risk activities be updated? Should advice be solicited from outside parties when updating the list? (Section II.F.2; pages 234-240)

80. Is this Secretarial list of minimal research activities a useful tool for the research community, or does it represent a loss of IRB flexibility in risk determination? (Section II.F.2; pages 234-240)
**Topic: Proposed Changes to IRB Operational Requirements**

81. What should IRBs consider when reviewing the plans for returning research results, for example, what ethical, scientific, or clinical concerns? (Section II.G.1; pages 241-247)

82. Is the §___.111(a)(3) and (b) focus on issues related to coercion or undue influence in research with vulnerable populations, and not other considerations related to vulnerability, appropriate? Note that this focus also appears in proposed §___.107(a). (Section II.G.1; pages 241-247)

83. Should pregnant women and those with physical disabilities be included in the category of subpopulations that may be vulnerable to coercion or undue influence? (Section II.G.1; pages 241-247)

**Topic: Proposed Revisions to IRB Operations, Functions, and Membership Requirements**

84. Should populations be considered vulnerable for reasons other than vulnerability to coercion or undue influence? Are the proposed categories appropriate? (Section II.G.2; pages 247-250)

**Topic: Proposal to Extend the Common Rule to All Clinical Trials (with Exceptions)**

85. Public comment is sought on whether there might be unintended consequences from the clinical trials expansion proposed in the NPRM in §__.101(a)(2)(i)). Unintended consequences may include an increase in burden or costs, or an inappropriate redistribution of costs. (Section II.H.1; pages 251-255)

86. Public comment is sought as to whether the criterion that the policy extends to all clinical trials conducted at an institution that receives federal support (see the NPRM at §__.101(a)(2)(i)) should be further clarified in some way. For example, should it specify a timeframe for support (e.g., within the past number of years), or a minimum monetary threshold value? (Section II.H.1; pages 251-255)

87. Public comment is sought on whether the definition of clinical trial (NPRM at §__.102(b)) should include additional explanation of what is encompassed by the term behavioral health related outcomes. (Section II.H.1; pages 251-255)

**Topic: Changes to the Assurance Process**

88. Would protection to human subjects in research be enhanced if OHRP conducted routine periodic inspections to ensure that the membership of IRBs designated under FWAs satisfy the requirements of §__.107? (Section II.H.2; pages 256-263)

**Topic: Department or Agency Discretion about Applicability of the Policy (NPRM at §__.101(c), (d), (i)) and Discretion Regarding Additional Requirements Imposed by the Conducting or Supporting Department or Agency (NPRM and current Rule at §__.124)** (Section II.H.3; pages 263-266) No request for comment.

**Topic: Research Covered by This Policy Conducted in Foreign Countries** (Section II.H.4; pages 266-267) No request for comment.

**Topic: Effective and Compliance Dates of New Rule** (Section II.I.1 pages 267-271)