The purpose of this document is to provide clarification to the recommendations forwarded by the Subcommittee on Research Involving Children (SRIC), and approved by the Secretarial Advisory Committee on Human Research Protections (SACHRP, also referred to as the "Committee") on November 1, 2005, March 14, 2006, and August 1, 2006. The majority of these recommendations involve subpart D (45 CFR 46.401-409) of the regulations at 45 CFR part 46. This is the final set of recommendations to be brought forward for the Secretary's review from the SRIC. Previous recommendations from SRIC that were approved by SACHRP were forwarded and approved by the Secretary on December 29, 2004 (contained recommendations related to 45 CFR 46.407) and March 10, 2006 (contained recommendations related to 45 CFR 46.404, 46.405, and 46.406). To facilitate the review of this document each section (e.g., 45 CFR 46.408, and 46.409) will start with the regulatory language for that part of the regulation followed by the individual verbatim recommendations relevant to that section and a brief summary of the discussions that occurred within SACHRP. As with all previous recommendations from SRIC that were approved by SACHRP, all recommendations provide clarification to existing regulatory language and, hence, do not require changes in the regulations.

1 Recommendations Related to 45 CFR 46.402/Assent

- **Present Regulatory Language (relevant sections only)**

§46.402 Definitions.

(b) "Assent" means a child's affirmative agreement to participate in research. Mere failure to object should not, absent affirmative agreement, be construed as assent.

- **Recommendation/Discussion**

1. *"When an IRB determines that the subject population is capable of assent, it should ensure that the protocol describes how assent procedures will meet the requirements of 45 CFR 46.402(b)."*

Discussion on Recommendation 1

This recommendation was presented and approved by SACHRP on November 1, 2005. The purpose of this recommendation is to provide IRBs with guidance on the issue of assent given by children participating in research. SACHRP felt that the IRB should require investigators to provide information on how the child assent process will be handled during the conduct of a proposed study. Specifically, the investigator must provide sufficient information to the IRB so that it can determine that a child's affirmative agreement to participate will be obtained if assent is sought. For example, a researcher proposes to draw blood from children and indicates in the protocol that the children will only be told that the blood draw will help researchers better understand how children's bodies work. In such a situation the IRB may also request that the investigator inform children that their participation is voluntary and obtain their affirmative agreement before initiating the procedure.

2. *"When the child's views may not ultimately be determinative, the investigator or parent/guardians should solicit the child's perspective without promising to follow*

his or her wishes. Investigators should only invite a child's decision about study participation when they intend to honor that decision. The practice of asking a child for a decision, then disregarding that decision if it conflicts with what the investigator or parents/guardians wish, is unacceptable."

Discussion on Recommendation 2

This recommendation was presented and approved by SACHRP on November 1, 2005. The purpose of this recommendation is to provide guidance to IRBs and investigators as to what they should consider relative to the dignity of the child subject when deciding whether to obtain assent. The Committee found the practice of asking a child for a decision and then disregarding it if it conflicts with the wish of the parents or guardians or the investigator to be unacceptable. It was felt a child's decision should not be requested unless it will be honored. The Committee felt this recommendation should apply to all research involving children.

3. *"Relative to documentation discretion for assent:*
   - *When the IRB determines that assent is required, it should also determine whether and how it should be documented. Often, IRBs require children's signatures because they think they have to; however, in many instances these signatures are developmentally inappropriate and therefore meaningless.*
   - *IRBs should use the discretion permitted in federal regulations for different documentation procedures (e.g., child's signature or documentation in investigator notes that assent was granted verbally) taking into account relevant state and local law.*
   - *To make such determinations, the IRBs should draw upon knowledge of the developmental level of the subject population and how different documentation procedures will best serve the goals of assent for particular research protocols and populations."*

Discussion on Recommendation 3

This recommendation was presented and approved by SACHRP on November 1, 2005. The purpose of this recommendation is to provide guidance to IRBs on the need for documentation of assent. It was felt by the Committee that this recommendation applies to all research conducted in children. Likewise, the Committee felt it is important for IRBs to be aware that it is not always appropriate for an IRB to require documentation of a child's signature for assent. Later in the public comment period it was noted that state and local law relative to the documentation of child assent should also be considered.

2 Recommendations Related to 45 CFR 46.408:

- **Present Regulatory Language**

§46.408 Requirements for permission by parents or guardians and for assent by children.

(a) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine that adequate provisions are made for soliciting the assent of the children, when in the judgment of the IRB the children are capable of providing assent. In determining whether children are capable of assenting, the IRB shall take into account the ages, maturity, and psychological state of the children involved. This judgment may be made for all children to be involved in research under a particular protocol, or for each child, as the IRB deems appropriate. If the IRB determines that the capability of some or all of the children is so limited that they cannot reasonably be consulted or that the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research, the assent of the children is not a necessary condition for proceeding with the research. Even where the IRB determines that the subjects are capable of assenting, the IRB may still waive the assent requirement under circumstances in which consent may be waived in accord with §46.116 of Subpart A.

(b) In addition to the determinations required under other applicable sections of this subpart, the IRB shall determine, in accordance with and to the extent that consent is required by §46.116 of Subpart A, that adequate provisions are made for soliciting the permission of each child's parents or guardian. Where parental permission is to be obtained, the IRB may find that the permission of one parent is sufficient for research to be conducted under §46.404 or §46.405. Where research is covered by §46.406 and §46.407 and permission is to be obtained from parents, both parents must give their permission unless one parent is deceased, unknown, incompetent, or not reasonably available, or when only one parent has legal responsibility for the care and custody of the child.

(c) In addition to the provisions for waiver contained in §46.116 of subpart A, if the IRB determines that a research protocol is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable requirement to protect the subjects (for example, neglected or abused children), it may waive the consent requirements in Subpart A of this part and paragraph (b) of this section, provided an appropriate mechanism for protecting the children who will participate as subjects in the research is substituted, and provided further that the waiver is not inconsistent with federal, state, or local law. The choice of an appropriate mechanism would depend upon the nature and purpose of the activities described in the protocol, the risk and anticipated benefit to the research subjects, and their age, maturity, status, and condition.

(d) Permission by parents or guardians shall be documented in accordance with and to the extent required by §46.117 of subpart A.

(e) When the IRB determines that assent is required, it shall also determine whether and how assent must be documented.

[**Note**: Several of the following recommendations also apply to waivers approved under 46.116(d). The regulatory language for this citation can be found in section 4 below.]

- **Recommendation/Discussion**

4. *"In considering the parent/guardian waiver under 45 CFR 46.408(c), IRBs should consider justifications for 'not a reasonable requirement' beyond the example of 'neglected or abused children' given within the regulation and include instances in which parental/guardian permission would jeopardize subject welfare or fail to provide additional subject protection."*

Discussion on Recommendation 4:
This recommendation was presented and approved by SACHRP on March 14, 2006 and November 1, 2005. The purpose of this recommendation is to provide IRBs with guidance on how they may interpret the regulations at 45 CFR 46.408(c) (waiver of parental permission). Essentially the Committee feels the IRBs can extend the waiver permitted under 45 CFR 46.408(c) to situations beyond "neglected or abused" children. The Committee wanted to provide IRBs with the flexibility needed to do important research on adolescents that could not be done if parental permission is required. This recommendation is linked with the next recommendation.

5. *Assuming that an appropriate mechanism for protecting the children is provided, the IRB may waive parental/guardian permission under 45 CFR 46.408(c) by applying the following three criteria:*
   - *The investigator has provided a reasonable argument that informing parents/guardians may result in harm to the child, or*
   - *The investigator has provided a reasonable argument that parental/guardian permission may not be in the child's best interest because of conflicts in parental/guardian role as it relates to the research, or*
   - *The research involves adolescents and:*
     a. *it is important to population health*
     b. *subjects have consent capacity*
     c. *participation is voluntary, and*
     d. *procedures are commensurate with State law.*

Discussion on Recommendation 5:
This recommendation was presented and approved by SACHRP on March 14, 2006. It may be important to note that a slightly different version of this recommendation was presented and approved by SACHRP on November 1, 2005. The purpose of this recommendation is to provide IRBs with guidance on how they may interpret the regulations at 45 CFR 46.408(c) (waiver of parental permission). The Committee felt that plausible arguments as to why informing the parents may be harmful to the child could include "conflicts in the parental role as it relates to research". These conflicts do not necessarily have to depict the parents as not good parents. An example of the application of criterion 1 would be an instance in which the investigator seeks to

identify patterns of psychological risk and resilience in high school students who consider themselves gay or lesbian, but who have not made this identity known to their parents or the public. The investigator might present literature on the social stigmatization of gay or lesbian youth, their potential confusion, and whether or not there is evidence of abusive reactions in particular populations. An example of the application of the second requirement would be an instance in which an investigator seeks to study coping behaviors of adolescents who have joined an Al-Anon Group. If there were only one parent and that parent was an alcoholic, there might be a conflict that would render the parent unable to make a decision in the child's best interest. A third example presented is one in which an investigator applies for a parental waiver to study adolescent girls' attitudes toward and use of different forms of birth control. Participants would be recruited from a clinic serving teenage girls 14 years and older who are permitted by state law to receive gynecology services and birth control without parental permission. To satisfy the third requirement, the investigator would have to show that the research is important to the health and well-being of adolescent females who are sexually active and provide empirical evidence demonstrating adolescents of this age are capable of understanding informed consent at adult levels. To satisfy the criteria the investigator must also assure that during recruitment it will be made clear to the teenagers that participation in the study is not related to their treatment and that a decision not to participate will not jeopardize their ability to get services. Finally, the investigator might show that asking subjects about their sexual practices and use of birth control is reasonably commensurate with questions asked during gynecology services they are permitted by law to receive without parental permission. Ultimately the Committee wanted to create a situation in which parental permission is not waived haphazardly just because a subject is an adolescent but rather support the notion that a waiver is acceptable provided the research interventions are the types of things that adolescents in a given state can go and get done, or evaluated, or treated for without their parents' permission. It is important to note that a waiver under 45 CFR 46.408(c) may apply to research involving risk greater than minimal whereas a waiver under 45 CFR 46.116(d) applies only to minimal risk research.

6. *"SACHRP re-affirms that:*
    - *Passive consent (in which parents/guardians are sent forms describing the research and asked to respond only if they do not want their child to participate) is not an approvable mechanism for satisfying the parent/guardian requirement under 45 CFR 46.116 or 45 CFR 46.408.*
    - *When parental/guardian permission meets the requirement for waiver under 45 CFR 46.116 (d) and 45 CFR 46.408 (c), an IRB should consider whether parental notification and right of refusal is appropriate."*

Discussion on Recommendation 6:
This recommendation was presented and approved by SACHRP on November 1, 2005. The purpose of this recommendation is to provide IRBs with guidance on the practice of what is often referred to as "passive consent" when obtaining parental/guardian permission for research involving children. The Committee felt it

was important to revisit the "passive consent fallacy" which assumes that parental failure to respond to consent forms sent home with the potential child-subject means that permission has been granted. The Committee felt this practice should not be permitted. This recommendation is intended to underscore the fact that when a "passive consent" process is utilized, the IRB/investigator is in fact applying a waiver (either under 46.408(c) or 46.116) of parental/guardian permission. As such, the investigator must demonstrate that a waiver is appropriate. An example of how this process could unfold includes the following: An investigator proposes to administer an after-school activity questionnaire to middle schoolers during health class. Participation is voluntary and adequate student assent will be obtained. Research is determined to be minimal risk and cannot be practicably carried out if parental permission is required. The IRB in this case could reasonably waive the requirement for parental permission under 45 CFR 46.116(d) although they might recommend a letter be sent home to the parents informing them about the research and providing a contact number if they had questions or did not want their child to participate.

3 Recommendations Related to 45 CFR 46.409

- **Present Regulatory Language**

§46.409 Wards.

(a) Children who are wards of the state or any other agency, institution, or entity can be included in research approved under §46.406 or §46.407 only if such research is:

(1) Related to their status as wards; or

(2) Conducted in schools, camps, hospitals, institutions, or similar settings in which the majority of children involved as subjects are not wards.

(b) If the research is approved under paragraph (a) of this section, the IRB shall require appointment of an advocate for each child who is a ward, in addition to any other individual acting on behalf of the child as guardian or in loco parentis. One individual may serve as advocate for more than one child. The advocate shall be an individual who has the background and experience to act in, and agrees to act in, the best interests of the child for the duration of the child's participation in the research and who is not associated in any way (except in the role as advocate or member of the IRB) with the research, the investigator(s), or the guardian organization.

- **Recommendation/Discussion**

7. *"A ward should be defined as a child who is placed in the legal custody of the State or other agency, institution, or entity consistent with applicable Federal, State or local law."*

Discussion on Recommendation 7:
This recommendation was presented and approved by SACHRP on August 1, 2006 and March 14, 2006. The purpose of this recommendation is to provide a useable

definition for wards which is not presently defined in 45 CFR part 46. The definition approved by the Committee is exactly the same definition used by the FDA (21 CFR 50.3(q)) hence it is consistent with the goal of harmonization. The Committee noted that it is sometimes challenging to identify who a ward is and to distinguish between who has physical custody of the child and who is responsible for providing medically-related permission for the ward. For example, often a child may be in a foster care home but legal custody may rest with the foster care agency and not with the foster parent. At the same time, the legally-recognized guardian may not be involved with the day-to-day life of the ward. Such issues contribute to the vulnerable nature of this population and should be considered by the IRB.

8. *"In approving the advocate for a specific protocol the IRB should take into consideration the following whether the advocate:*
   - *has appropriate education and training, in order to take into consideration the nature of the research and the expectations of the advocacy role.*
   - *has the ability to make a determination regarding each ward's participation in research that is independent and free of any contractual requirements or financial gains or other conflicts that depend upon the number or types of subjects required for recruitment, enrollment, and ongoing participation.*
   - *has independence from the research for the entire period of the advocacy role.*
   - *can act in the interests of protecting the safety and welfare of the ward by assuming an intermediary role between the child, investigator, guardians, and the IRB. This may include, as appropriate, meeting with wards, biological parents, foster parents, and researchers as deemed necessary, having the time and ability to become familiar with the child's health, behavior, social and physical environment, and notifying the investigator and IRB of any concerns about the child's participation in research."*

Discussion on Recommendation 8:
This recommendation was presented and approved by SACHRP on August 1, 2006. The purpose of this recommendation is to provide IRBs with guidance on what criteria they should consider when approving an advocate. The Committee did not want to be prescriptive and noted that not all criteria needed to be satisfied in all situations. Basically, this recommendation suggests the IRB consider whether the proposed advocate will (1) understand the ward's situation, (2) be able to have some kind of individual contact with the ward so that they can make appropriate decisions in the ward's best interest, and (3) be sufficiently independent from research influence, that is, they are not being paid to enroll a certain number of wards, etcetera. Although not articulated in the recommendation, the Committee felt the role of the advocate could include, among other possible activities, (1) decision making about whether the ward should even be approached in order to participate in research, (2) determining that the approach is not coercive, (3) assuring assent is voluntary, (4) ensuring the ward's right to withdraw from research is respected and (5) monitoring the ward's status (including guardianship) during the conduct of the research. Despite these roles the Committee noted that the advocate does not necessarily have a legal role in providing "consent" when there is a legal guardian. The thought is that the advocate is an additional voice to

speak on the child's behalf given that the legal guardian is often removed from the day-to-day care of the child. Additionally, the advocate can provide continuity to the child's participation in research when there are changes in the child's caregiver situation (e.g. change in foster parents). As an observer of the child's participation in research the advocate should be empowered to approach the investigator and the IRB to express any concerns they may have about the child's participation in research. Finally, the Committee felt that although an advocate should get paid for their services, the level of compensation provided should not be dependent upon recruitment goals (e.g., tied to head count).

9. *"In reviewing research that falls within category §46.404 and §46.405 and includes or will potentially include wards, the IRBs may consider the inclusion of additional safeguards to protect the rights and welfare of these subjects in accordance with the provisions of subpart A section §46.111(b). This may include actions such as the appointment of an advocate or any other safeguard deemed necessary to protect the safety and welfare of the ward taking into consideration the nature of the research."*

Discussion on Recommendation 9:
This recommendation was presented and approved by SACHRP on August 1, 2006. The purpose of this recommendation is to provide IRBs with guidance on additional protections they may consider providing to wards who are participating in research meeting the criteria for 45 CFR 46.404 (no greater than minimal risk) and 45 CFR 46.405 (greater than minimal risk but prospect of direct benefit). The HHS regulations do not require that the protections at 45 CFR 46.409 be applied to §46.404 and §46.405 level research. However the regulations at 45 CFR 46.411(b) permits the IRB to consider any "additional safeguards" for vulnerable populations (including wards) they deem appropriate. Essentially, this recommendation suggests to IRBs that they consider applying the protections described under 45 CFR 46.409 to §46.404 and §46.405 level research if they feel it is appropriate.

10. *Two parts:*
    - *"If an individual child/adolescent becomes a ward while participating in research that falls under category §46.406 or §46.407, the requirements of section §46.409 must be implemented in order for the ward to continue participation."*
    - *"If an individual child/adolescent becomes a ward while participating in research that falls under category §46.404 or §46.405, the IRB may consider requiring additional safeguards to protect the safety and welfare of the ward as specified in subpart A section §46.111(b)."*

Discussion on Recommendation 10:
This recommendation was presented and approved by SACHRP on August 1, 2006. The purpose of this recommendation is to remind IRBs and investigators of their responsibility to apply the protections under 45 CFR 46.409 to any child participating in a §46.406[1], or §46.407[2] level research protocol that subsequently becomes a ward

[1] Research meeting the threshold of 46.406 involves greater than minimal risk and no prospect of direct benefit to the individual subjects, but is likely to yield generalizable knowledge about the subject's disorder or condition.

after initial enrollment. Additionally the IRB should consider additional protections permitted under §46.111(b) for children participating in §46.404 and §46.405 level research who subsequently become wards after enrollment. The underlying rationale for this recommendation is a concern that when a child becomes a ward of the state while participating in research, the legally recognized decision-maker may change. Informed consent is an ongoing process and as a result, the logistics of who decides and the implications of continued research participation may also change. It was noted by the Committee that an advocate would not be expected to know the ward *a priori* the child's participation in the research however the advocate should have the ability to know the ward when needed.

11. *"If an IRB reviews a protocol for which the investigator may reasonably anticipate that some subjects may become wards during the course of the research and the research falls into category §46.406 and §46.407, the IRB may consider reviewing and approving the protocol in accordance with §46.409. This would include identifying a potential advocate in the event one is needed."*

Discussion on Recommendation 11:
This recommendation was presented and approved by SACHRP on August 1, 2006. The purpose of this recommendation is to provide IRBs with guidance on how they may handle the review of protocol in which there is a reasonable possibility that enrolled children may become wards of the state during the course of the study. The underlying rationale for this recommendation is that this effort at the initial review may reduce unnecessary delays or interruptions in the research and the subject's participation if a subject were to subsequently become a ward. This recommendation is meant to be permissive by allowing IRBs to perform a "409 contingency review". It should be noted that the Committee felt that any advocate proposed in the contingency plan need not know the child who become a ward *a priori* hence it is possible to designate an advocate who has no present knowledge of the children participating in the research in the "409 contingency plan". However once a child become a ward the advocate should in some manner become aware of the child's situation including possibly meeting the child.

12. *"Institutions and their IRBs, in collaboration with other operating units (e.g., office of legal counselor legal counsel), should provide guidance and education to investigators and their associated research personnel regarding:*
    - *who is defined as a ward of the state in accordance with state regulations*
    - *specific State regulations and requirements if they exist*
    - *the need to notify the IRB when a ward is initially considered for research in category §46.406 and §46.407 research*
    - *the need to notify the IRB when a child/adolescent already participating in research categorized as §46.406 and §46.407 becomes a ward of the state."*

Discussion on Recommendation 12:

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[2] Research meeting the threshold for 46.407 involves research not otherwise approvable by the IRB but presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children.

This recommendation was presented and approved by SACHRP on August 1, 2006. The purpose of this guidance is to recommend that IRB develop guidance and provide education to investigators on the topic of wards participation in research. The underlying principle is that it was felt that investigators are not well informed on this issue. The recommendation intentionally does not state how this should be done. The Committee noted that such guidance and training could be web-based and/or consist of workshops although it would be up to the individual IRBs and institutions. Relative to this recommendation the Committee noted that when a component analysis of the study found that one arm or procedure of the research falls within Category 406 or 407, and other arms or procedures are approvable under 45 CFR 46.404 or 45 CFR 46.405, the most protective component will govern and the research needs to be reviewed and approved in accordance with the provisions of 45 CFR 46.409.

4 Recommendations Related to Subpart A Issues

- Present regulatory language (relevant sections only)

§46.116 General requirements for informed consent.

(d) An IRB may approve a consent procedure which does not include, or which alters, some or all of the elements of informed consent set forth in this section, or waive the requirements to obtain informed consent provided the IRB finds and documents that:

(1) The research involves no more than minimal risk to the subjects;
(2) The waiver or alteration will not adversely affect the rights and welfare of the subjects;
(3) The research could not practicably be carried out without the waiver or alteration; and
(4) Whenever appropriate, the subjects will be provided with additional pertinent information after participation.

- **Recommendations/Discussion**

13. "To determine that a parent/guardian waiver 'will not adversely affect the rights and *welfare of the subjects' under §46.116(d) the IRB should consider*

- *Federal, state, or local laws pertaining to parental/guardian permission*
- *alternative mechanisms to protect the rights and welfare of child participants, **and***
- *when appropriate, whether the investigator has adequately considered the norms of the community from which subjects will be drawn."*

Discussion on Recommendation 13:
This recommendation was presented and approved by SACHRP on March 14, 2006. The purpose of the recommendation is to provide IRBs guidance on what factors should be considered when determining whether or not a parental/guardian waiver under 45 CFR 46.116(d) would adversely affect the rights and welfare of the child subject. Examples of state and federal laws that should be considered include Health Insurance Portability and Accountability Act (HIPAA), the Protection of Pupil Rights Amendment (PPRA) and the Family Education Rights and Privacy Act (FERPA) to

name a few. Alternative mechanism could include a situation in which the investigator provides adequate procedural protections to ensure that child's assent to participant is informed and voluntary or there might be an independent participant advocate depending upon the need of the subject population. Norms to be assessed are those from the community which the children are recruited. Consideration of local norms might be assured, for example, by having an unaffiliated nonscientific IRB member who knows the community speaks to the issue or by engaging a consultant. The Committee felt it would be the responsibility of IRBs to determine the adequacy of the information provided on community norms. An example of an approvable request for a waiver would be a survey on soft drink and fast food intake in which the investigator has worked with the local PTA to develop procedures to ensure that participation is voluntary. In such a situation it would be expected that middle school children who will participate are old enough to understand assent information and no laws would be violated. On the other hand, a waiver could not be granted if the investigator wanted to correlate eating patterns with student grade point averages, since the Family Educational Rights and Privacy Act (FERPA) does not permit access to school records without parental consent. Another example of a reason not to grant the waiver would be concern from an Orthodox Jewish community about questions related to pork. Under the 4th bullet, the "when appropriate" was added in order to not be too prescriptive and to give IRBs flexibility. It is important to note that the Committee felt the investigator has the primary obligation to provide a sufficient argument to the IRB to satisfy this recommendation.

14. *"To determine whether parental/guardian permission can be waived under §46.116(d)(3) because the research cannot be 'practicably carried out', the IRB should require the investigators to provide:*
    - *a reasonable argument that scientific validity would be compromised if parental/guardian permission was required*
    - *a reasonable argument that alternative methods to obtain parent/guardian permission are not feasible, and*
    - *a rationale for why the research could not be conducted with a population for whom parental/guardian permission could be practicably carried out.*

Discussion on Recommendation 14:
This recommendation was presented and approved by SACHRP on March 14, 2006 and November 1, 2005. The purpose of this recommendation is to provide IRBs with guidance as to what conditions may an IRB consider when waiving parental/guardian permission or child assent consistent with the phrase "could not be practicably carried out without the waiver" (45 CFR 46.116(d)(3)). The Committee felt there should be adequate justification provided by the investigator to permit a waiver of parental permission under 45 CFR 46.116(d)(3) although not all three bulleted items above need to be satisfied in all cases. The choice of "alternative methods" would be based upon the nature, risks and purpose of the activities described in the protocol. It was noted during the discussion that the recommendation would not support waivers driven solely by cost and convenience but would not exclude the concerns from consideration. The intent of the recommendation is not to create a situation in which

the IRBs mentor investigators in appropriate research design. Ultimately the burden of this recommendation is on the investigator who must provide the IRB with the appropriate information to make a determination. An example in which the permission of a parent or guardian could be waived under this recommendation would be an instance in which the investigator proposes to waive parental permission for a national study of diet and after-school activities to predict census tract concentrations of middle school children's respiratory disease. To meet the requirement for scientific validity, a large random sample of children is necessary for statistical power. In regard to alternative methods, census tract neighborhoods vary with respect to ability to contact parents through telephone directory or other measures; therefore, data would not be evenly spread out across the census tracks without the waiver. All census tracts must be included for data to be meaningful.

15. *"Parental/guardian permission should never be waived under §46.116(d)(3) for convenience nor waived solely for reasons of cost or speed or other expedient measures if doing so weakens protection of subjects' rights and welfare."*

Discussion on Recommendation 15:
This recommendation was presented and approved by SACHRP on November 1, 2005. The purpose of this recommendation is to provide IRBs with guidance as to what limitations should be applied when granting a waiver of parental/guardian permission or child assent under the concept of what is practicable. The Committee wanted to ensure there were clearly understood limitations on the use of waivers granted because research would otherwise not be "practicable." For example, IRBs may not waive parent/guardian permission because of funding limitations if those limitations result in procedures that do not provide the same degree of subject protections that better funded research would provide.

16. *"In evaluating whether assent should be waived under §46.116(d) for research involving no greater than minimal risk, the IRB may consider the following:*
    - *research involves no greater than minimal risk*
    - *requirements for parental/guardian permission have been met,*
    - *waiver of assent does not violate Federal, State, or local law,*
    - *The study could not be practicably conducted (e.g. scientific validity would be compromised without the waiver), and*
    - *The PI has presented evidence that alternative methods to obtain assent are not feasible.*

Note: Even when child assent is waived, the IRB should consider explaining the research to the child and the right of refusal"

Discussion on Recommendation 16
This recommendation was presented and approved by SACHRP on November 1, 2005. The purpose of this recommendation is to provide IRBs with guidance on approving waiver of assent under 45 CFR 46.116(d). Ultimately the recommendation is intended to be an interpretation of the existing regulations that shows how an investigator might think about meeting the requirement. The Committee agreed there

are times when child assent may be waived but parental/guardian permission is not. Similarly the Committee felt that "scientific validity" is really only one example of an instance in which assent is not practicable. An example of assent waiver under 45 CFR 46.116(d) could include a situation in which an investigator proposes a randomized study to assess whether providing adolescents with sample written questions pertaining to high risk behaviors they may be involved with affects the nature and number of questions the adolescents asks of their care provider. The Committee felt such research would involve no greater than minimal risk and would meet the requirements for waiver of parent/guardian permission. In this situation no state, federal or local law is violated and scientific validity would be compromised without the waiver because randomization would not be possible. Finally the investigator provides evidence that alternative methods to obtain assent are not feasible since assent information would create response bias. In this case the Committee agreed it would be reasonable for the IRB to consider and reject requiring explanation of the research to the child and the right of refusal (i.e. assent).