# ATTACHMENT A

## DETERMINATION OF MINIMAL RISK FOR CHILD RESEARCH

Derived from a presentation by: Celia B. Fisher, Ph.D., and Susan Z. Kornetsky, M.P.H. [5th Report for SACHRP Consideration Clarifying 45 CFR 46 Subpart D Definitions - January 31, 2005](http://www.hhs.gov/ohrp/archive/sachrp/mtgings/mtg01-05/present/fisher_files/frame.htm)

## Reference Point for Uniform Definition

• The definition of “minimal risk” at 45 CFR 46.102(i) when applied to Subpart D should be interpreted as those risks encountered by normal, average, healthy children living in safe environments in daily life or during the performance of routine physical or psychological examinations or tests.

## Minimal Risk Should be Age indexed

• Evaluation of minimal risk under Subpart D should be indexed to the risks in daily life and routine medical and psychological examinations experienced by children the same age as the subject population.

## Upper Limits of Risk & Harm

• The uniform, age-indexed definition of minimal risk should represent the upper not lower limits of risk to which children can be exposed under §46.404.

Rationale: Research procedures should not fall under §46.404 for children who because of health or other reasons would be at greater risk of harm from procedures which are minimal risk for normal, average, healthy children living in safe environments.

## Equivalent Procedures

• Procedures that are equivalent in probability and magnitude of harm to risks of daily life or routine physical or psychological examinations or tests experienced by average, healthy, normal children living in safe environments should be considered as consistent with the definition of “minimal risk.”

## Equivalence Criteria

• Is the probability and magnitude of harm equivalent in:

duration

cumulative characteristics reversibility of harm

to risks of daily life or routine examinations

## Examples of Well-Child Procedures [From April, 2005 SACHRP presentation; IOM, 2004; 4.9-4.10]

* Physical examinations
* Measurement of height, weight, head circumference
* Assessment of obesity with skin-fold calipers
* Collection of blood or voided urine
* Measurement of heart rate and blood pressure
* Hearing and vision tests
* Modest changes in diet or schedule
* Testing of fine and gross motor development
* Non-invasive physiological monitoring
* Medical and social history
* Psychological examinations or tests
* Guidance and education (for the child, the parents, or both)

## Routine Psychological Tests Indexed to Standardized Screening or Assessment Measures

* Child and adolescent intelligence tests
* Infant mental and motor scales
* Educational tests / Reading and math ability tests
* Neurological or motor disorders
* Social development
* Family and peer relationships
* Emotional regulation
* Feelings of sadness or hopelessness

## DETERMINATION OF MINOR INCREASE OVER MINIMAL RISK FOR CHILD RESEARCH

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## Determining Minor Increase Over Minimal Risk

* Applying a uniform procedure for assessing whether a research presents a minor increase over minimal risk requires evaluating the risk along 10 different criteria.
* Rationale. Methods, compounds, instruments and other research procedures are so variable that a single quantitative unit of increase cannot be uniformly applied. However, there is a uniform process of evaluation that can be applied.

## List of Uniform Criteria for Determining a Minor Increase Over Minimal Risk

1. Minimal Risk Comparison
2. Scientific Evidence of Risk
3. Certainty of Evidence
4. Documented Harms
5. Equivalence of Procedures
6. Participant Perspectives
7. Mitigating Factors
8. Inclusion/Exclusion Criteria
9. Monitoring
10. Safety & Competence

## 1. Minimal Risk Comparison

* The procedure does not meet minimal risk criteria
* The probability and magnitude of harm or discomfort anticipated in the research is greater than those ordinarily encountered by normal, average, healthy children living in safe environments in their daily activities or during the performance of routine physical or psychological examinations or tests.

## 2. Scientific Evidence of Risk

* There is peer reviewed scientific evidence of the range of risks associated with the procedure for the subject population, OR
* The procedure is sufficiently similar to other interventions with well characterized risks that prudent, informed judgments about risks can be made.

## 3. Certainty of Evidence

* The extent and quality of the evidence is such that there is little uncertainty about the range of risks involved.
* Lack of sufficient data for a risk profile would create a higher level of uncertainty supporting a more conservative approach to judgments that a procedure is only a minor increment over minimal risk

## 4. Documented Harms

* The documented harms are not serious for the subject population
* The data indicates no or an extremely small probability of risk of major complications.
* Harms associated with the procedure do not require in-patient monitoring or follow-up evaluation (for the procedure itself)
* The harms if they occur are transient and reversible

## 5. Transient & Reversible

* Transient: Restricted to time of procedure or short post-experimental period
* Reversible: Procedure to reverse the effect requires no more than a short-term simple clinical intervention

## 5. Equivalence of Procedures

• The procedures are equivalent in risk to documented risk profiles in terms of

1. Duration of harm or discomfort and
2. Cumulative effect of procedures on the probability and magnitude of harm.

## 6. Participant Perspectives

• Whenever possible the data includes information about the subject population’s experience of the procedures (e.g., painful, anxiety producing).

## 7. Mitigating Factors

• The procedure reflects consideration of documented mitigating factors known to minimize or exacerbate the risk.

## 8. Inclusion/Exclusion Criteria

• Subject inclusion and exclusion criteria reflect consideration of documented subject characteristics that may moderate the probability and magnitude of harm of the procedure.

**9. Monitoring**

• There is an adequate monitoring procedure.

## 10. Safety & Competence

• The procedure will be performed in a safe environment by qualified personnel with experience conducting the procedure with the subject population.