

LETTERS

Nontherapeutic Research and Minimal Risk

In his article "Nontherapeutic Research, Minimal Risk, and the Kennedy Krieger Lead Abatement Study" (Nov-Dec 2001), Dr. Robert Nelson concluded that some children participating in the Kennedy Krieger Repair and Maintenance Study were exposed to greater than "minimal risk" and, since there were no direct benefits to participants, that therefore the study should not have been approved by the IRB under 45 CFR 46.404.

Nelson acknowledged that the blood tests for lead monitoring were properly considered minimal risk under §46.404. The study investigators had provided information to the IRB, based on previous work, that appropriate protections would be in place during the lead reduction procedures to protect families from lead dust that may be associated with repairs, and that the lead reduction methods would not result in increased background lead levels for families living in the repair and maintenance (R&M) homes. The information provided by the investigators also demonstrated that the lead reduction methods would reduce lead dust in vacant homes, so that participants living or moving into the R&M homes would be exposed to less lead in the home than they were experiencing in their daily lives prior to participation in the study. It should be noted that the study did not include a "control" group of families moving into homes without any intervention aimed at reducing lead levels. Therefore, the IRB correctly concluded that the study interventions (i.e., blood draws and lead reduction methods) did not result in risk to subjects.

Thus the central question is whether "continued exposure" to any lead in the home should be considered a risk of the study or part of the condition being studied. Nelson argued

that there were two distinct populations of children: "those children living in a home selected for abatement (and thus already 'at risk' for lead toxicity) and those children moving into a selected home after scheduled abatement (and thus placed 'at risk' for lead toxicity)." While it is correct that 50% of families moved into R&M homes after they had already undergone one of the lead reduction interventions, the record shows that all of the families in the R&M homes lived in or came from existing housing that contained lead paint hazards. Furthermore, it should be recognized that lead in the home was not the only source of lead exposure. Other potential sources included lead in other buildings, the soil, and water. That is, all subjects who participated in the study were already "at risk" from lead in the environment and this risk was independent of study participation. The IRB concluded that continued exposure to lead (i.e., the condition being studied) is a consequence of living in an inner city, and therefore "intentional exposure to lead" was not part of the study. Since the risks from the interventions directed at the R&M houses and blood level monitoring were not considered to represent more than minimal risk, the IRB was justified in approving the study under §46.404.

If all homes were constructed without lead paint, or there were funds available to perform comprehensive lead abatement on existing homes, there would have been no need for the study. Except for houses built after 1978, when laws were enacted that prevented the use of lead paint, there was no community standard for any kind of lead abatement in existing homes. There were few funds available for lead abatement or reduction from other sources if families stayed in or moved into nonimproved homes and did not participate in the study. Therefore there were few realistic alternatives for moving into housing that was lead free or had complete

lead abatement. Nelson agreed that for families living in homes contaminated with lead (a description that applies to all of the families in the R&M homes), it might have been the best option for them to be in the study. Furthermore, he agreed that the study might have been approvable under §46.407, which requires review by the Secretary of HHS. His argument was that the IRB should not have approved the study under the minimal risk definitions of §46.404. We don't believe that the risk of lead exposure, which is intrinsic to living in old housing in Baltimore, was a risk of the study. Indeed, with the R&M improvements any risk of living in old housing in Baltimore was reduced. For these reasons, we believe that the approval by the IRB was appropriate.

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Robert Nelson replies:

The experimental lead abatement procedures used in the Kennedy Krieger (KKI) Repair and Maintenance Study offered the prospect of direct benefit to those children living in the lead-affected homes, regardless of whether those procedures are considered minimal risk. Although the risk was minimized, the claim that the lead abatement procedures are minimal risk assumes either (1) the IRB should only evaluate the incremental risk caused by the research intervention (as argued by the Johns Hopkins University IRB) or (2) minimal risk should be judged in the context of the daily life of the children enrolled in the study. First, the assessment of incremental risk needs to consider appropriate protections from lead dust raised during the abatement procedure, and the risks of not performing a complete lead abatement (which is one hypothesis of the study). Reasonable people may disagree whether the incremental risk was

minimal risk. However, for those children already living in lead-affected homes, the prospect of direct benefit from the partial lead abatement procedures would justify exposure to more than minimal risk. Second, minimal risk should be interpreted to refer to the socially allowable risks to which an average, normal, healthy child is routinely exposed. Although continued exposure to lead may be the unfortunate (and perhaps unfair) result of socioeconomic circumstances, this increased level of risk should not be interpreted as minimal risk. Questions remain whether moving into a lead-affected home was a study intervention; and whether continued lead exposure should be considered a "condition" for all children in the KKI study.

Should moving into a vacant home that underwent an experimental lead abatement procedure be considered a study intervention? The presence of a young child in such a home appears necessary to answer the study's primary hypothesis. If it is true that landlords were encouraged to rent these homes to families with young children, the IRB should consider moving children into such homes a study intervention. As lead exposure is not minimal risk, the intervention must offer the prospect of direct benefit (§46.405) or present only a minor increase over minimal risk for a child with a "condition" (§46.406). Can moving into the home be considered a direct benefit for those children not already living in the partially lead-abated homes? The empirical claim that all of the children who moved into the abated homes were exposed to less environmental lead than prior to study participation can only be made after the study is complete. In addition, living in a lead-affected home may be considered a "condition" only as a result of the actual choices available to and made by parents. The claim that parents of these children would have no other alternative but to move into lead-affected homes may have statistical support given the Baltimore housing market. However, can we be certain that any given parent would not

choose to look for other housing once fully informed of the alternatives? If the consent document disclosed the risks of lead, and the alternative to move into housing either built after 1978 or completely lead abated, perhaps we could be more confident in this claim. The evidence made public suggests that these risks and alternatives were not disclosed as part of the consent process for this study. The risk of lead exposure from the environment (excluding a child's home) may define a "condition." However, the level of this environmental risk (and thus whether it is a "condition") was one hypothesis of the study and the answer did not require moving children into the lead-abated homes.

The central point in dispute appears to be whether a parent's decision to move a child into a home that underwent an experimental lead abatement procedure should either be considered a study intervention, or an inclusion criterion for defining a child's condition. The continued discussion of these (and other) issues is important for the refinement of the special protections for children in research. Unfortunately, many of us (myself included) can only comment from the documents available in the public domain. I applaud the Johns Hopkins Bayview Medical Center IRB for engaging in this discussion and ask that the documents necessary for a full evaluation of this protocol be made public as soon as possible.