Lessons Learned From the Children's Environmental Exposure Research Study

We examined 5 different ethical concerns about the Children's Environmental Exposure Research Study and make some recommendations for future studies of exposure to hazardous environmental agents in the home.

Researchers should seek community consultation and participation; make participants aware of all the risks associated with the research, including hazards discovered in the home and uncertainties about the risks of agents under investigation; and take steps to ensure that their studies will not have unfair representation of the poor or people of color.

Researchers should also avoid even the appearance of a financial conflict of interest in studies that are likely to be controversial and make it clear to all parties that studies will not intentionally expose subjects to hazardous environmental agents. (*Am J Public Health.* 2007;97:414–418. doi:10.2105/AJPH.2005.081729)

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THE CHILDREN'S

Environmental Exposure Research Study (CHEERS) became embroiled in controversy in the fall of 2004, when environmental groups charged that the study was unethical. CHEERS' critics argued that the study had a number of different ethical problems, including: (1) the study intentionally exposed children to pesticides, (2) the study targeted low-income people of color, (3) the incentives to participate in the study amounted to coercion or undue influence, (4) private sources of funding for the study were unacceptable conflicts of interest, and (5) the parents were not provided with enough information about pesticides during the consent process.[5,6]

In response to these accusations, the Environmental Protection Agency (EPA), the main sponsor of CHEERS, suspended the study pending further review by an independent committee of scientists and ethicists. (CHEERS had already been approved by a special EPA committee and institutional review boards at Battelle Memorial Institute, the University of Florida, and the Florida Department of Health; the neurobehavioral part of the study had been reviewed by the University of North Carolina institutional review board.)

The EPA's response did not satisfy special interest groups or politicians, who pressed for the study to end. Senators Barbara Boxer (D, Calif) and William Nelson (D, Fla) grilled EPA administrator nominee Stephan Johnson during his nomination hearing and threatened to derail his confirmation if he did not stop the study.[1] On April 8, 2005, Johnson cancelled CHEERS. In making the decision, Johnson maintained that CHEERS had been grossly misrepresented by the media and advocacy groups.[2] Many scientists were disturbed that Congress had intervened in the peer review process and that the study had become a political football used by politicians to score points among constituencies and special interest groups.

This was not the first time in recent years that research on environmental hazards in the home has come under intense scrutiny. In 2001, a Maryland appellate court ruled that researchers from the Kennedy Krieger Institute, who were conducting a study of lead abatement methods in Baltimore homes, had legal duties to warn the plaintiffs of unsafe lead levels detected in the blood of children and to obtain informed consent. The court also rendered opinions about the risks that children are legally permitted to face in research and the scope of researchers' legal duties toward human subjects in nontherapeutic research.[3] The Kennedy Krieger Institute case, which instigated legal and bioethical debates about environmental health and pediatric research, was prominently featured in a report released by the Institute of Medicine in 2005, *Ethical Considerations for Research on Housing-Related Health Hazards Involving Children.*[4]

We describe the CHEERS protocol, examine these allegations concerning the design and implementation of CHEERS, and make some recommendations for future environmental health research.

THE PROTOCOL

The goal of CHEERS was to measure in-home exposures to pesticides and other chemicals in 60 children younger than 3 years of age and to understand how age and activities affect exposures.[7–9] Knowledge about the effects of human exposure to pesticides is derived primarily from animal dosing studies and observational studies on adult men and women. Although there is some knowledge about the pesticide exposures of children living in agricultural communities,[10] little is known about children's exposures in the home.[8,11] It is important to understand the risks that pesticides pose to children, because children may be more sensitive to pesticides than adults, because of their developing organ systems, lower ability to detoxify chemicals, and increased exposure to pesticides from dermal contact, respiration, and ingestion.[8] Scientists do not know whether the EPA's current pesticide regulations provide adequate protection for children.

CHEERS would have enrolled children living in Duval County, Florida, not attending day care and living in a home with high

levels of pesticide use; less than 10% of the participants would live in homes with low pesticide use. The researchers planned to distribute posters and flyers at Duval County Health Department clinics, pediatrician's offices, schools, churches, stores, and 3 hospitals. Research staff would spend 3–4 hours per day conducting screening interviews at the Duval County Health Department clinics. Parents of potential participants could also contact a toll-free phone number to obtain more information. After the initial screening interview, research staff would immediately schedule a home visit.

During this visit, researchers would take surface wipe samples to confirm the respondent's eligibility, obtain information about pesticides and cleaning products used in the home, explain the study activities in more detail, and obtain written consent from the participant's parent. Participants would receive up to $970 and promotional items, such as bibs and t-shirts, to complete the study. Parents were also given a video camera, which they would also be allowed to keep, to use to record activities that could expose their children to pesticides.

Investigators planned to collect data concerning chemical exposures and activities during their visits to the homes of participants. Following the initial screening visit, the study would have conducted data collection and sampling during 6 monitoring events over a 2-year period. Each monitoring event would involve 5 3-hour visits to the home, for a total of 30 home visits to complete the study. Investigators had planned to interview parents and obtain urine, air, soil, and surface-wipe samples. Parents would assist in the data collection by recording their pesticide and antimicrobial purchases during the 2 years of the study, observing and videotaping their child's activities during the monitoring periods, keeping a food diary during the monitoring period, and collecting samples of food, hand wipes, and urine. Each child would wear an electronic activity monitor around the ankle during the monitoring period. The investigators would also inform parents about following manufacturers' instructions for pesticide use and warn them about any dangerous pesticide exposures. Although most of the parents would be chosen because they used pesticides, they could remain in the study even if they decided to reduce or eliminate their pesticide use; they would also be free to withdraw from the study at any time.

CHEERS was classified as a minimal-risk study with minimal benefits to participants (federal agencies do not treat financial incentives as benefits). The protocol did not mention any physical risks to participants, because the participants were not asked to change their normal household routines. The protocol mentioned social or legal risks from breach of confidentiality, as well as data security measures and application for a Certificate of Confidentiality. Potential benefits to the participants included obtaining information about pesticide levels in their homes and ways to reduce exposures to toxic chemicals and pollutants at home.[8]

The agencies sponsoring CHEERS included the EPA, the Centers for Disease Control and Prevention, and the Duval County Health Department, which helped to recruit subjects and served as a community liaison.[7] The American Chemistry Council (ACC) gave the EPA a $2.1 million grant to expand CHEERS to collect data on exposures to chemicals, such as phthalates and flame retardants, present in consumer products. The EPA and the ACC signed a cooperative research and development agreement.[7]

INTENTIONAL DOSING OR OBSERVATIONAL STUDY?

One objection to CHEERS was that it deliberately exposed children to pesticides. Although CHEERS was not designed as an intentional dosing study, many people mistakenly viewed it us such. This view stems in part from an article published in the *Chemical Engineering News*, which stated that "parents must agree to spray or have pesticides sprayed inside their homes routinely during the two-year study period, and will receive up to $970 for participating."[12(p10)] Other newspapers, television news shows, and websites portrayed CHEERS as an experiment on children. EPA scientists asked the *Chemical Engineering News* to correct its misrepresentation, but the correction was never made (L. Sheldon, PhD, EPA, personal communication, July 18, 2005).

An intentional dosing study is a controlled experiment in which researchers administer chemicals to participants using a specific dosing schedule and measure its metabolic and physiologic effects. Pesticide companies have submitted data to the EPA from human dosing studies, but CHEERS had no direct connection to this research.[13] CHEERS was an observational study designed to measure children's exposure to pesticides in the home. In an observational study, researchers collect data on exposures that occur in the course of routine activities. For example, many studies have measured the effects of pesticides on agricultural workers.[14]

The most significant ethical difference between observational studies and intentional dosing studies is that observational studies have low risks, while intentional dosing studies may not. In an observational study, risks could come from collecting blood, from a distressing interview, or from disclosure of private information. In an intentional dosing study, risks also include exposing the subjects to the chemical under investigation, which may be significant, depending on the type of chemical being tested, the dosage, and the route of administration.

Critics argued that CHEERS was like an intentional dosing study because it gave parents an economic incentive to start using pesticides.[5] Some of the flyers distributed by the CHEERS investigators stated that only families that use pesticides would be eligible for the study.[15] These flyers could have given parents the impression that they would need to start applying pesticides to be in the study. The EPA attempted to correct this impression with later public information distributions, including the *CHEERS Fact Sheet*.[7] As noted previously, the EPA had established a screening process to ensure that parents would be excluded from the study if they had not been previously using pesticides in the home.

First, the EPA could have reduced the potential for misunderstanding by stating that parents should not change their use of pesticides because of the study and by indicating in promotional materials that participants would

be free to decrease or stop their use of pesticides while participating in the study. Second, the agency could have asked community members and other interested parties to carefully review the materials used to publicize CHEERS. The perspective of community members can be very important, because community members may notice problems that investigators and institutional review board members overlook.[4,16]

Although collaboration with the Duval County Health Department was considered a form of community involvement, it was not sufficient to build the trust necessary for conducting a community-based study like CHEERS. Local residents may not view health departments as representing the interests of community members. Allowing community organizations to assist with research design and implementation can help to build trust and enhance the quality of research.[16]

TARGETING GROUPS ON THE BASIS OF RACE AND CLASS

Another criticism is that CHEERS targeted low-income people of color.[5] The study protocol stated that Duval County was chosen for the study on the basis of evidence of high pesticide use in Duval County, not on the demographic composition of the county. The EPA did not specify race, income, or ethnicity as eligibility criteria for participation. However, the Duval County Health Department was the primary community partner for the study, and CHEERS would have recruited parents in 6 Duval County Health Department clinics where, in 2000, 75% of users of pregnancy services had incomes below the federal poverty line, and only 1.8% had incomes greater than twice the federal poverty level. Three hospitals that agreed to help recruit participants reported that 47.5% of births were to Blacks, compared with 35.7% for the 7 major county hospitals combined. The EPA could have taken some steps to increase the participation of higher-income and White families, such as establishing relationships with institutions that serve wealthy families and recruiting participants from those institutions.

FINANCIAL INCENTIVES

Another ethical concern was that the financial incentives for participation were excessive, especially when considering most of the families would have low incomes. The ethical problem with paying participants too much money is that this can invalidate the consent process by leading to undue influence.[17] Federal research regulations do not offer any guidance on the amount of money to pay research participants, but they do require researchers to minimize the possibility of coercion or undue influence when obtaining consent.[18] Undue influence could occur if financial incentives undermine the participant's ability to weigh benefits and risks.

An appropriate amount to pay participants depends on several factors, including the amount of time, inconvenience, or risk involved in the study, and the socioeconomic characteristics of the study population. The payment of $970 may have been a fair rate for participation, given the amount of time, labor, and inconvenience involved in the study. To receive the $970, the parents would need to participate in 30 3-hour home visits, take a survey, make videotape recordings, monitor their child's activities, and keep journals. All of these tasks would have required about 150 hours of the parents' time, or $6.47 per hour, slightly above the federal minimum wage of $5.15. Some studies pay participants anywhere from $5 to $400 per hour, depending on the amount of time, inconvenience, and risk involved in research participation.[19]

We have not tried to resolve the question of whether the incentives in the CHEERS study were too large or too small.[20] We have noted, however, that the determination of an appropriate level of compensation, especially when potential study participants have low incomes and little financial stability, requires obtaining input from members of that community. Better consultation with members of the affected community might have avoided some of the questions about the financial incentives in the study.

CONFLICT OF INTEREST

Critics also charged that the ACC's $2 million contribution to the study created an unacceptable conflict of interest for the EPA. A conflict of interest in research is a situation in which the investigator's personal, professional, or financial interests are likely to bias his or her judgment. Institutions can also have conflicts of interest in research if they have financial interests that are likely to bias their collective decision-making.[21] Because researchers and institutions have a variety of interests, avoiding all conflicts of interest, or apparent conflicts, in research is usually not a realistic option. In most cases, disclosing or managing financial or other interests will be the best strategy for dealing with conflicts of interest.[22] In more problematic cases, prohibition or avoidance may be the best response.[23]

We found no evidence that CHEERS investigators had any financial or other relationships with the ACC or pesticide or chemical companies. However, the EPA had a financial relationship with the ACC, which represents chemical companies (not pesticide companies). Critics argued that the relationship with the ACC would bias the results of CHEERS, because the organization would take steps to influence the study. We found no evidence that the ACC or any private company directly influenced CHEERS' research design, data analysis, or dissemination plans. The ACC did suggest that the researchers study household chemicals in addition to pesticides, but it made no attempt to suggest how researchers should decide upon the sample size, inclusion criteria, procedures, or other aspects of research design. To their credit, the CHEERS researchers resisted an attempt by CropLife America, an organization that represents pesticide companies, who tried to influence the study by asking that pesticides be removed from the study (L. Sheldon, PhD, EPA, unpublished letter, 2004).[24]

While there is no direct evidence that sponsorship by the ACC biased the study, the relationship between the ACC and the EPA created the appearance of bias, and thus, the appearance of a conflict of interest. Given the controversial nature of pesticide use, the sensitivity of research on vulnerable populations, and the importance of building public

trust, the wisest course of action would have been to refuse industry sponsorship.

PROBLEMS WITH THE CONSENT PROCESS

Other concerns were raised about the informed consent procedures, because they did not provide the parents with enough information about the hazards of pesticide use in the home.[6] The first version of the informed consent documents did not mention the reason why it would be important to study children's exposures to pesticides (i.e., that pesticides are dangerous, and the "safe" exposure level for children is not known). The revised version of the consent form adds a clarifying sentence stating that "One of the underlying premises of the study is that pesticides are toxic substances, the effects they can have on children are unknown, and the doses that are harmful are unknown."[24(p2)]

However, the consent documents did not provide parents with specific information about the potential dangers to infants and toddlers of pesticide use in the home. Research suggests that young children are highly susceptible to adverse physiological, behavioral, and cognitive effects of toxic agents because of their developing neuroendocrine and immune systems, lack of fully developed detoxification processes, small body size, and large relative intake of air, food, and water.[11] In addition to factors that affect young children's susceptibility to toxins in general, pesticide application in the home presents concerns because of the proximity of children's breathing zones to floors where pesticides are applied, their potential for dermal uptake and contamination of garments through crawling, hand-to-mouth behavior, and pica (eating nonfood substances, such as dirt).

All this was well known to the researchers, yet they made no plans to inform the parents that scientists firmly believed that infants and toddlers were at higher risk from exposures than were adults and older children. Furthermore, there were great uncertainties about the impacts of pesticide exposures on humans in this age range, in part because the complex cognitive and behavioral impacts of these exposures could not be fully and adequately evaluated with animal or in vitro studies. Parents should have been provided with this information to decide whether to enroll in the study, withdraw from the study, or decrease their pesticide use while remaining in the study. Community consultation would have helped researchers to deal with the challenge of developing a consent form that provided subjects with the appropriate type and amount of information, written at the appropriate reading level.

The lack of plans to inform parents about the special risks to their young children could also have put the parents themselves at risk. If parents later learned about the increased susceptibility of young children, they could have suffered psychological distress, remorse, or worse, especially if their children did later have learning disabilities, behavioral problems, or physical health problems, all of which are great public health concerns in the Black community. Even though they had used pesticides prior to being invited to be in the study, they could blame themselves for continuing to use pesticides and for participating in the research, possibly motivated in part by the monetary incentive. After participating in such a study, parents might be more aware of this topic and more attuned to public information or possible future news accounts about impacts of environmental toxins on children.

OTHER ETHICAL CONCERNS

Another ethical concern arises from the CHEERS protocol for collecting information on children's neurobehavioral performance in order to test methods for a future study. Despite these plans, the protocol specified that relationships between pesticide uptake and neurobehavioral measures would not be analyzed. Because so little is known about neurobehavioral effects on young children exposed to low levels of pesticide, investigators should have planned statistically efficient repeat-measures longitudinal analyses to evaluate evidence of a relationship while being clear about the limitations of sample size.

Finally, the acronym *CHEERS* is ironic and potentially offensive. There is nothing cheerful about potential health effects of children's pesticide exposures.

CONCLUSIONS

So what can we learn from CHEERS? We have offered some points to consider in studies of exposure to hazardous environmental agents in the home. Researchers should seek community consultation and participation in studies, such as those researching dangers in home environments, that will have a substantial impact on the community; researchers need to make participants aware of all the risks associated with the research, including hazards discovered in the home, uncertainties about the risks of agents under investigation, and the susceptibilities of vulnerable populations.

Researchers should take steps to ensure that their studies will not have unfair representation of the poor or people of color. They should also avoid even the appearance of a financial conflict of interest in studies that are likely to be controversial. Finally, researchers should take great care in research design and implementation to make it clear to all parties that studies will not intentionally expose participants to hazardous environmental agents. ■

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Contributors

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Human Participant Protection

No institutional review board approval was required for this analysis.

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