IMPROVING ASSESSMENT OF THE EFFECTS OF ENVIRONMENTAL CONTAMINATION ON HUMAN REPRODUCTION

REPORT OF THE WORKING GROUP ON
HUMAN REPRODUCTIVE OUTCOMES

CHILD TRENDS, INC.

Improving Assessment of the Effects of Environmental Contamination on Human Reproduction

REPORT OF FINDINGS AND RECOMMENDATIONS

The Working Group on Human Reproductive Outcomes

Child Trends, Inc.
2100 M Street, NW
Suite 411
Washington, DC 20037

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EXECUTIVE SUMMARY

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Report of Findings and Recommendations

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Public concern with potential environmental hazards is high. Almost daily there are newspaper accounts of chemical spills, radiation leaks, improperly disposed waste materials, air pollution, and contaminated water. There are also frequent allegations of excessive numbers or clusters of poor reproductive outcomes, such as miscarriages or birth defects, in particular communities or populations. The Environmental Protection Agency (EPA) -- the agency generally turned to by concerned citizens -- currently has no standard way to determine whether a community may indeed have unduly high rates of adverse reproductive outcomes. A major obstacle to a more coherent response by EPA has been uncertainty over how to evaluate the validity of the different claims. Efforts to make such evaluations are hindered by a lack of high quality national data that could serve as a benchmark against which local rates could be compared.

In 1985, EPA and the National Science Foundation provided grant funds to Child Trends, a non-profit research organization in Washington, D.C., to form a panel of experts that would recommend several approaches EPA might take to improve its ability to assess whether environmental contamination is causing reproductive health problems for U.S. citizens. The Working Group on Human Reproductive Outcomes was composed of a diverse set of specialists from a variety of fields, including: epidemiology, human genetics, obstetrics, pediatrics, reproductive toxicology, survey research, and sampling statistics. A number of federal agencies were also represented at the Working Group meetings.

The decision to focus on undesirable reproductive outcomes grew out of a recognition that reproductive health problems have received considerably less attention at EPA than cancer, respiratory diseases, and other disorders that can be associated with environmental contamination. Yet reproductive problems and birth defects are of great concern to the public. Negative reproductive outcomes almost always pose emotional costs to the individuals affected, and often entail considerable financial burdens as well. In addition, birth defects carry substantial

societal costs. Apart from the costs of the reproductive problems themselves, improved tracking of changes in reproductive outcomes over time and across geographical areas could prove to be advantageous in alterting the public to the development of dangerous environmental conditions. Many agents that are associated with reproductive problems can also be expected to be associated with other health effects. And the time period between exposure and the occurrence of a miscarriage or birth defect is usually shorter than the latency period for the development of diseases such as cancer. Thus, an effective means of detecting changes in reproductive outcomes could serve as an early warning system for other health hazards as well.

As a result of their deliberations, the following recommendations were developed by the panel, together with governmental specialists and Child Trends staff:

1. The Environmental Protection Agency should make use of existing federal surveys of the U.S. population to develop baseline data on the incidence and prevalence of reproductive problems among women living in different types of communities and among those from different age and ethnic groups.

2. The Environmental Protection Agency should provide matching funds to state health agencies to encourage the development and improvement of birth defect monitoring systems in the states. These activities should be coordinated with efforts that are currently supported by the Center for Environmental Health of the Centers for Disease Control.

3. The Environmental Protection Agency should initiate discussions with other federal agencies to explore the feasibility of setting up a jointly-funded network of birth hospitals that would provide high-quality continuing data on birth defects in a representative sample of U.S. births.

4. The Environmental Protection Agency should develop standard questionnaires and local survey methods that can be used to determine what the incidence and prevalence of negative reproductive outcomes in a given area really are. These procedures should parallel those used in federal surveys, such as the National Survey of Family Growth.

5. The Environmental Protection Agency should provide support for basic research aimed at improving our ability to establish causal links between environmental pollution and reproductive problems. This should include research to improve the assessment of exposure to specific environmental contaminants in humans, and of early fetal loss, as well as animal studies of reproductive impairments.

These recommendations and the considerations behind them are presented in detail in the accompanying report.

Improving Assessment of the Effects of Environmental Contamination on Human Reproduction

REPORT OF FINDINGS AND RECOMMENDATIONS

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INTRODUCTION

Public concern with potential environmental hazards is high. The case of Vernon, New Jersey, provides one example of such concern. According to a report in The New York Times of July 24, 1985, residents of Vernon fear that radiation from satellite-communication antennas is causing an abnormally high level of birth defects and miscarriages in their town (Friendly, 1985). The Environmental Protection Agency (EPA) and the Centers for Disease Control (CDC) have been called in to explore the validity of these fears.

Vernon, New Jersey is not an isolated case, of course. Almost daily there are newspaper accounts of chemical spills, radiation leaks, improperly disposed waste materials, air pollution and contaminated water. There are also frequent allegations of excessive numbers or clusters of poor reproductive outcomes, such as miscarriages or birth defects, in particular communities or populations, as well as fears of higher than expected rates of certain types of cancer and other diseases. The relationships between environmental contamination and health effects are often unclear, however, and concerned citizens frequently request that studies be done to determine whether environmental pollution is causing health problems in their communities.

EPA, the agency generally turned to by concerned citizens, currently has no systematic procedures or guidelines for coping with these requests. Such requests are apt to be received by regional offices, and these offices usually act autonomously in an ad hoc manner in responding to them. The lack of coordination between regional and federal offices, as well as the ad hoc approach to these serious health questions, have been a source of dissatisfaction both within EPA and to communities around the United States. A major obstacle to a more coherent response by EPA has been uncertainty over how to evaluate the validity of the different claims. Efforts to make such evaluations are hindered by a lack of high quality national data on many of the health outcomes of interest. Such data are needed to serve as benchmarks against which local rates can be compared.

GOALS OF THE WORKING GROUP ON HUMAN REPRODUCTIVE OUTCOMES

In 1985, EPA and the National Science Foundation provided grant funds to Child Trends, a non-profit research organization in Washington, D.C., to form a panel of experts that would recommend several approaches EPA might take to improve its ability to assess whether environmental contamination is causing reproductive health problems for U.S. citizens.

The Working Group on Human Reproductive Outcomes was composed of a diverse set of specialists from a variety of fields, including: epidemiology, human genetics, obstetrics, pediatrics, reproductive toxicology, survey research, and sampling statistics. A number of federal agencies were also represented at the working group meetings, including the Environmental Protection Agency, the National Center for Health Statistics, the Centers for Disease Control, and the Division of Maternal and Child Health of the U.S. Public Health Service. Members of the Working Group and agency representatives are listed at the end of this report.

The charge to the panel was to focus on the statistical data needed to clarify the association between environmental contamination and undesirable reproductive outcomes. More specifically, the Group was asked to suggest ways to improve data on poor reproductive outcomes. They were not asked to deal with the equally vexing problem of improving data on human exposure to environmental contaminants. Undesirable reproductive outcomes include the following:

- non-voluntary infertility or subfecundity; (Infertility is the inability to conceive a pregnancy after one year of unprotected intercourse. Subfecundity is a more general term that includes couples for whom it may be difficult, but not impossible, to conceive.)
- miscarriages/spontaneous abortions; (These terms refer to pregnancies that end in embryonic or fetal death before the 20th or 28th week of the pregnancy, depending on the definition.)
- stillbirths; (This term refers to pregnancies that end in a fetal death after the 20th or 28th week of pregnancy, depending on the definition.)
- birth defects in live or stillbirths; (This refers to any of a number of abnormal conditions ranging from major chromosomal disorders, such as Down's syndrome, to minor abnormalities such as birthmarks.)

- low birthweight, prematurity, intrauterine growth retardation, and other signs of difficulties, such as low Apgar scores, in live births. (Infants weighing less than 2,500 grams [or about 5 1/2 pounds] at birth are said to be low birthweight infants. Infants born live prior to 37 weeks of pregnancy are said to be premature. Babies who are small for their gestational age are said to have experienced intrauterine growth retardation. Low birthweight is typically a symptom of birth prematurity and intrauterine growth retardation. Apgar scores, named for Dr. Virginia Apgar, who devised these scales, are assessments of the infant's heart rate, respiratory rate, muscle tone, cry, and color at birth to summarize the baby's physical condition. The scores are typically taken at 1 and 5 minutes after birth.)

The decision to focus on undesirable reproductive outcomes was made for several reasons. First, reproductive health problems have received considerably less attention at EPA than cancer, respiratory diseases, and other disorders that can be associated with environmental contamination. Yet reproductive problems and birth defects are of great concern to the public. All of these negative outcomes pose emotional costs to the individuals affected, and often entail considerable financial burdens as well. In addition, birth defects carry substantial societal costs. They account for a large proportion of child hospitalizations, sickness, and deaths (Edmonds et al, 1981). Researchers have estimated that the future costs of custodial care only for children born in 1978 with serious birth defects could run more than two billion dollars (Selle et al, 1979).

Apart from recognizing the costs of the reproductive problems themselves, improved tracking of changes in reproductive outcomes over time and across geographical areas could prove to be advantageous in alterting the public to the development of dangerous environmental conditions. This is because many agents that are associated with reproductive problems can also be expected to be associated with other health effects. And the time period between exposure and the occurrence of a miscarriage or birth defect is usually shorter than the latency period for the development of diseases such as cancer. Thus, an effective means of detecting changes in reproductive outcomes could serve as an early warning system for other health hazards as well. Of course, in order to understand the causes of any changes in rates of undesirable reproductive outcomes, data on exposures to environmental contaminants, occupational hazards, drugs, etc. would also be needed.

EPA'S NEEDS AND THE DIFFICULTIES OF OBTAINING ADEQUATE DATA

In order to be able to determine whether negative reproductive outcomes are unusually high in a given area, EPA needs good national baseline data on the outcomes of interest, data that can be analyzed according to a variety of individual characteristics such as race and age. Good baseline data do not currently exist, however. Measurement problems are a major reason for the lack of high quality data. Current methods of mandatory reporting, such as birth certificates, are seriously flawed because of underreporting and inaccurate reporting. The following illustrate some of the difficulties in obtaining good baseline data:

- Many miscarriages go unrecognized even by the women experiencing them. This is particularly true of very early miscarriages.

- Even miscarriages that are recognized by women may go unreported, particularly if there are no complications, either because the women may not seek medical attention or because the physicians may not report the miscarriages.

- Specific birth defects are relatively rare. Consequently it is necessary to follow a large number of births to obtain stable estimates of the baseline rates of occurrence.

- The frequency with which birth defects are found varies with the time of ascertainment; some defects are not usually recognized at birth, while others often occur in stillbirths or neonatal deaths and will be missed in surviving infants.

- The diligence and experience of the observer who is recording the birth defect can affect the quality of the data. Less experienced observers are likely to miss more subtle birth defects.

- New technologies, such as amniocentesis, chorionic villi sampling and other antenatal procedures that detect fetal abnormalities, could alter the pattern of birth defects and miscarriages in years to come. Problematic pregnancies may be terminated and thus never enter a birth defects registration system or be counted among miscarriages. These technologies would affect rates over time and make trend analyses difficult.

- Differences in the health-related behaviors and demographic characteristics of women may account for a large proportion of the variation in the probability of miscarriages and birth defects. Thus, changes in the behavior or in the characteristics of childbearing women may also influence variation in negative outcomes.

- Recorded miscarriages are only a subset of all miscarriages and may have different causes than those that go unrecorded.

- There may be multiple explanations for specific negative reproductive outcomes; many or most will not be clearly attributable to specific environmental contaminants.

- There may be different contaminants affecting the same population at the same time.

- Length or amount of exposure may be a critical factor in producing negative outcomes, yet it will not always be possible to determine the extent of exposure. For cases like Three Mile Island or chemical spills, the timing is well specified. In other cases, however, timing of exposure may be difficult to ascertain. In fact, a rise in negative reproductive outcomes may be the first indication of contamination.

Another problem confronting EPA is that, from a methodological point of view, it is important that local area estimates of undesirable reproductive outcomes be comparable to the national benchmark data. For the data to be comparable however, identical questions and identical methods of collection need to be used. Actually collecting comparable data in local areas could be difficult, though, particularly in communities where citizens are already concerned about the incidence of adverse reproductive outcomes.

DATA FROM EXISTING FEDERAL SYSTEMS ON REPRODUCTIVE OUTCOMES ARE INADEQUATE

There are two major federal systems that attempt to monitor reproductive outcomes: the Centers for Disease Control's Birth Defects Monitoring Program (BDMP) and the National Center for Health Statistics's Vital Registration System. Although both programs have merit, they also have serious limitations as far as the needs of EPA are concerned.

Birth Defects Monitoring Program

The Birth Defects Monitoring Program compiles hospital discharge data for approximately 1200 U.S. hospitals with obstetrical services. These hospitals are self-selected from a set of hospitals that use the same medical auditing system. Information on birth defects is obtained from machine-readable hospital records at the time the infant is discharged after delivery. The BDMP was started in December 1974 by the Centers for Disease Control with the aid of start-up grants from the

National Institute for Child Health and Human Development and the National Foundation -- March of Dimes. The BDMP is the largest single source of data on malformed newborns in the United States. From EPA's perspective, however, its limitations include the following:

- It is not a representative sample of births in the U.S.
- The data are not well-defined geographically -- that is, the proportion of births covered varies substantially across regions of the country and participating hospitals in a given state or area are not necessarily representative of all births in that state or area.
- There is no quality-control mechanism to insure that different hospitals diagnose and classify defects in a uniform manner.
- There is no coverage of early miscarriages.
- There is little or no information on important variables such as length of residence in an area, occupation, smoking history, etc. Thus important exposure information is missing.
- There is no opportunity for prospective tracking of pregnancies and their outcomes.

U.S. Vital Registration System

The National Center for Health Statistics (NCHS), Division of Vital Statistics, collects and publishes natality and mortality data that are provided by the states. All states have participated in this registration system since 1933. Although the birth statistics data in the Vital Registration System capture nearly 100 percent of births occurring in the United States, the data do have the following limitations for EPA's purposes:

- Birth defects are significantly underreported on birth certificates, and the degree of underreporting varies across different types of defects. (A proposed new standard birth certificate with an itemized list of defects may improve the quality of birth defects reporting for some defects -- particularly those that are recognizable at birth -- but there is still likely to be significant underreporting, because birth certificates are usually filled out before some types of defects are detected.)
- There is no quality-control mechanism to insure that physicians in different states and counties diagnose and classify defects in a uniform manner.

- Reporting of fetal deaths are affected by differences in state regulations and county practices.
- There is no coverage of early miscarriages.
- Although there are data on usual residence, there is no indication of duration at that location.
- There is no opportunity for prospective tracking of pregnancies and their outcomes.
- There is usually a lengthy time delay in NCHS reporting of birth defects data.

SPECIFIC RECOMMENDATIONS

To improve the capacity of EPA to assess whether and how environmental contamination is affecting reproductive health in the U.S. population, the following recommendations were developed by panel members, together with governmental specialists and Child Trends staff members.

1. <u>The Environmental Protection Agency should make use of existing federal surveys of the U.S. population to develop baseline data on the incidence and prevalence of reproductive problems among women living in different types of communities and among those from different age and ethnic groups.</u>

These data can serve as benchmarks against which rates of miscarriage and infertility in areas of known or suspected environmental contamination can be evaluated. The primary source of data on reproductive impairments is the National Survey of Family Growth. Other useful, though more limited data sources are the National Longitudinal Survey of Labor Force Participation, the National Health and Nutrition Examination Survey, and other federal studies of maternal and child health.

The National Survey of Family Growth (NSFG) represents the best available source of national data on infertility and miscarriage. However, the existing survey has important limitations for use in environmental studies. Although the overall number of women surveyed is large (e.g., 7,969 women of ages 15-44 were interviewed in Cycle III of the NSFG in 1982), the number in a particular geographic area is considerably smaller (ranging in NSFG III from less than 80 to over 400 cases per area). This means that estimates of rates of reproductive impairments in particualr areas will have fairly large standard errors. Moreover, there is no guarantee that geographic areas of especial environmental interest will fall into the sample. And some important information for environmental studies, such as the woman's length of residence in the area, is lacking from existing rounds of the survey. Despite these limitations, the

quality of the sample design, questionnaire construction, and survey field work is high and much useful data can be extracted from the NSFG files.

In order to derive the most benefit from federal survey data, the following steps should be taken by EPA:

a. Analyze existing survey data on miscarriages and infertility and tabulate these data in ways that would facilitate comparisons with data from areas of suspected contamination. (For example, tables could be developed that show the number of cases of miscarriage that would be expected in a given time period in communities of different size, location, and demographic composition, along with the standard errors of these estimates.)

b. Merge existing county- and metropolitan area-level data on levels of air and water pollution and concentrations of toxic waste with federal survey data on miscarriages and infertility in order to examine ecological correlations between pollution levels and rates of reproductive impairment. (The strength of the relationships uncovered in these analyses will be limited by the quality of the available environmental pollution data and by the fact that survey sampling points are apt to be somewhat removed from pollution monitoring sites. Nevertheless, the low cost of the proposed analyses, and the paucity of population-based studies linking reproductive outcomes to environmental exposures make it worthwhile to exploit these existing data as outlined above.)

c. Buy additional questions on future rounds of the National Survey of Family Growth, questions that would make the data on miscarriages and infertility more useful for EPA's purposes. (For example, questions could be included on how long the woman has lived in the present area and where she lived and worked in the months immediately preceding and during any earlier pregnancies. Questions about a limited number of specific and more prevalent birth defects might also be added to expand the range of outcomes covered in the NSFG.)

d. Sponsor an enlargement of the sample size on future rounds of the National Survey of Family Growth in order to produce more stable estimates of the rate of reproductive problems in various areas and segments of the population.

It should be noted that EPA has proposed to the Bureau of the Census that a short sequence of questions on reproductive problems be included in the 1990 Census. Whether such a sequence will be included appears doubtful at this time, since no appropriate measures were included in the major Census pre-test. The possibility should certainly be pursued and, in

addition, EPA should sponsor methodological research to evaluate how well reproductive problems can be measured with such a short sequence of questions.

2. The Environmental Protection Agency should provide matching funds to state health agencies to encourage the development and improvement of birth defect monitoring systems in the states. These activities should be coordinated with efforts that are currently supported by the Center for Environmental Health of the Centers for Disease Control.

This approach would build on existing state efforts and cooperative agreements between the states and the Centers for Disease Control. At present, 12 states (Arkansas, Arizona, California, Illinois, Kansas, Maryland, Nebraska, New Jersey, New York, Virginia, Washington, West Virginia) have passed laws mandating birth defects surveillance programs and have programs in place or under development. Four more (Florida, Iowa, Michigan, and Missouri) have some type of surveillance program in place, although no state law specifically requires it. At least fifteen additional states have begun to develop legislation requiring such surveillance, or are discussing various approaches to the monitoring of birth defects.

The advantages of working with the states to improve and expand birth defects monitoring are the following:

- No one can predict with certainty where environmental contamination problems will occur, so a system that provides prospective data for virtually all areas of the country is highly desirable.

- Given the low rates at which specific types of birth defects occur, very large samples of births are needed to provide reliable indications of change over time in rates of occurrence. (Even some individual state systems may not be large enough and may have to be combined with data from other states.)

- If a state monitoring system is already in place, and the system contains information that permits each birth to be associated with a specific residential location, it becomes a relatively simple matter to determine whether rates of birth defects seem to be elevated in an area of suspected contamination.

- A cooperative monitoring effort involving both state and federal agencies reflects the shared responsibility that state and federal authorities have for dealing with public health emergencies. Such an approach is also consistent with the current administration's policy of shifting more governmental responsibility to the states.

Developing a complete network of state monitoring systems could well be a costly proposition, however. Assuming a relatively modest federal contribution of $50,000 per state per year, approximately $3 million per year would have to be spent by EPA over several years in order to produce significant movement toward nationwide registry of birth defects. Given the amount of interest states are already showing in monitoring systems, however, smaller investments by EPA could probably stimulate the development of some new state monitoring systems or improvement in existing systems. In order to get such a program underway in an efficient manner, EPA might choose to make selective investments in exemplary surveillance programs in states that have already begun to develop high-quality data collection programs. Cooperative funding with other agencies would also reduce the amounts EPA would be required to invest. The less EPA invests, though, the less control it will have over the types of data collected.

There are, in any case, a number of problems that would have to be addressed before such a network could entirely meet EPA's needs. The major concern of the panel was with the quality of the data collected by the state programs. There has been little effort to assess the accuracy or completeness of coverage of existing state systems, or to institute quality control programs that would increase the validity of the birth defects data. Furthermore, some existing state systems rely only on birth certificate information and thus have the known underreporting problems of such data. Many of these states, however, are planning to expand their programs as soon as they have the resources to do so. The feasibility of federal-state cooperation in this area is demonstrated by the fact that the Centers for Disease Control already have cooperative agreements with Iowa, New Jersey, and Washington to develop prospective monitoring for birth defects. All three agreements call for analyzing the association between birth defect rates and environmental contamination. The funding for these agreements is provided by Superfund via the Agency for Toxic Substances and Disease Registry.

EPA, in conjunction with the Centers for Disease Control, the National Center for Health Statistics, the National Institute of Environmental Health Sciences, and other cooperating federal agencies, would have to provide technical assistance and financial incentives to state agencies to get them to standardize their monitoring procedures and upgrade the quality of their surveillance systems. The federal agencies should set up a national clearinghouse and data improvement center to coordinate these efforts. As part of the clearinghouse function, standardized codes of birth defects and a list of diagnostic criteria for each type of defect should be developed.

Even with improved data quality and broader geographic coverage, state monitoring systems, as currently constituted,

would not provide information on miscarriages or infertility. EPA would also have to develop a strategy for assessing reproductive effects in states that choose not to establish monitoring systems or are slow to develop such systems.

3. The Environmental Protection Agency should initiate discussions with other federal agencies to explore the feasibility of setting up a jointly-funded network of birth hospitals that would provide high-quality continuing data on birth defects in a representative sample of U.S. births.

Current state monitoring systems and the BDMP rely upon existing hospital records and/or birth certificates. Several panel members felt that in order to insure the collection of high-quality data on birth defects, it is necessary to go beyond hospital record-keeping and vital registration systems and have specially trained data collection personnel in hospitals that provide obstetrical services. Advantages of such an approach include better standardization in diagnoses, more uniformity with regard to the age at which diagnoses are made, and the ability to include chromosome studies on more infants. It would not be necessary to install trained personnel in all birth hospitals (although this would be an eventual goal if a nationwide defects registration system were to be established). Valid data on baseline levels and changes over time in the overall frequency of specific birth defects could be collected through a network of at least 450 participating hospitals, chosen so as to produce a valid probability sample of at least 10 percent of all U.S. births and take advantage of locally available expertise or existing programs.

Such a system would also be relatively costly to operate (requiring perhaps $2 million per year), but it could be implemented more rapidly than a network of state monitoring systems. It would not provide data on occurrences of defects in all localities, but it could be used to supply other national data of interest to a broad range of federal health agencies, including the Food and Drug Administration; the Occupational Safety and Health Administration; the Division of Maternal and Child Health of the Public Health Service; the Institute of Environmental Health Sciences; and the National Institute of Child Health and Human Development. If these agencies were to participate with EPA in the funding of such a data collection system, the cost to each agency would be substantially reduced.

In addition to providing trend data more quickly than a full state monitoring system, the hospital-based system could assist the states in assessing and improving the quality of their state surveillance systems. The specialized personnel in the hospitals could also collect more detailed and accurate data on environmental and occupational exposures, antenatal diagnostic procedures, reasons for fetal deaths, and birth defects in stillborns, as well as birth defects in live newborns. This system would not provide information on miscarriages or infertility.

4. The Environmental Protection Agency should develop standard questionnaires and local survey methods that can be used to determine what the incidence and prevalence of negative reproductive outcomes in a given area really are. These procedures should parallel those used in federal surveys, such as the National Survey of Family Growth.

Survey methods could be used by EPA or local health authorities to investigate possible reproductive health effects in areas of known contamination. They could also be used when a question has been raised by local citizen groups about apparently high rates of reproductive problems in an area of suspected contamination. The survey methods would be employed to verify that the local rates of impairment are indeed as high as claimed and are not merely due to peculiarities of population composition or to spurious sampling or counting procedures.

Without standard methods for determining rates of miscarriage and infertility, it is not possible to make valid comparisons between rates in a given geographical area and rates in other areas or in the nation as a whole. Standard survey methods will not in themselves establish whether or not there is a causal link between environmental contamination in an area and reproductive problems in that area. But such methods do make it possible to detect or confirm elevated rates of impairment with greater accuracy and sensitivity.

One problem that standard survey methods will not completely eliminate, however, is the possibility of differential reporting in areas where anxieties are high because of publicity about environmental contamination and/or clusters of adverse reproductive outcomes. For this reason, EPA should sponsor research to identify and develop measures that are more robust in the face of widespread public concern.

With regard to the type of outcomes covered, survey methods are most suitable for the measurement of miscarriages and infertility. They are more problematic with regard to the measurement of birth defects because of possible respondent unfamiliarity with diagnostic terminology. It may well be possible, however, to use survey methods to collect data of adequate quality on a limited number of relatively clear-cut and readily apparent types of defects. The major problem would be the large sample size needed for a sample of the general population to generate estimates of sufficient precision for these rare events.

5. The Environmental Protection Agency should provide support for basic research aimed at improving our ability to establish causal links between environmental pollution and reproductive problems. This should include research to improve the assessment of exposure to specific environmental contaminants in humans, and of early fetal loss, as well as animal studies of reproductive impairments.

Although the primary charge to the Working Group was to focus on baseline statistical data and methods for determining whether an area has an excessive rate of negative reproductive outcomes, members of the group felt strongly that EPA and related agencies should be investing in the basic reserch needed to improve the scientific capability to establish causal connections between environmental contamination and reproductive disorders. Three areas of methodological research that appear promising in this respect are: 1) passive monitoring devices and biochemical tests for measuring a family's exposure to specific environmental contaminants; 2) biochemical methods for early detection of ovulation, pregnancy, and pregnancy loss; and 3) studies of reproductive outcomes in animals.

Developmental work is needed to perfect methods for field measurement of the actual exposure that family members have had to specific pollutants in the environment. This includes the development and application of monitoring devices that can be left in the home or worn on the person over a period of time to ascertain ambient levels of specific pollutants. The use and improvement of biochemical tests on bodily tissues and fluids should also be encouraged. Such environmental measures could be used in conjunction with the measures of reproductive outcome described above, although it will not always be possible to apply the exposure measures on a prospective basis.

Physiological research has shown that many human fetal losses occur in the very early stages of pregnancy, before the woman may even be sure that she is pregnant and/or that a miscarriage has occurred. Because these early fetal losses occur at a relatively high rate compared to later losses, there is the potential that the measurement of such losses might prove to be more sensitive than current methods for monitoring the reproductive health of a population. Some studies have already been conducted using biochemical methods for longitudinal monitoring of pregnancy and early fetal loss in small samples of volunteers. There is, however, still great ignorance on the extent, nature, and causes of early pregnancy losses. Moreover, the detection of such losses involves major logistical problems for even small basic research projects. Therefore, it may be some time before these methods can be usefully applied in population-based studies of reproductive hazards.

Animal studies of negative reproductive outcomes provide several advantages. Inasmuch as animals and humans share the same environment (air, water, soil), for a given environmental contaminant, animal reproductive outcomes may parallel human

reproductive outcomes (infertility, early pregnancy loss, stillbirth, malformation). Moreover, it may be easier to quantify exposure in animals than in humans and to control for potentially confounding variables. Longitudinal research may be more feasible than in humans, since there are captive populations of animals (e.g., farm animals, kennels) that can be followed relatively easily.

In areas with few human pregnancies, animal studies may identify specific outcomes occurring at elevated frequencies (e.g., specific patterns of malformations). Also, the shorter intergenerational interval of animals permits more rapid assessment of the potential effects of an environmental contaminant on the reproductive fitness of offspring exposed in utero (e.g., infertility). Of course, results from animal studies cannot always be extrapolated to humans. However, consistency of human and animal data supporting an association between an environmental contaminant and a reproductive outcome strengthens the biological plausibility of the association.

SUMMARY AND CONCLUSIONS

In summary, the Working Group on Human Reproductive Outcomes finds existing systems for monitoring the reproductive health of the U.S. population to be unsatisfactory. Also unsatisfactory are current federal procedures for responding to local concern about possible environmental threats to reproductive function. The panel recommends that the Environmental Protection Agency act in conjunction with other relevant agencies to develop and implement standard methods for assessing whether local rates of infertility, miscarriage, stillbirth, and birth defects are elevated; and to strengthen baseline data against which local reproductive data can be evaluated.

Significant improvements in the monitoring of infertility, miscarriages and stillbirths may be achieved at modest cost by taking the steps outlined in this report. These steps include:

- making better use of existing federal survey data on infertility and miscarriage;
- adding questions and increasing sample sizes on future rounds of the National Survey of Family Growth; and
- developing standard questionnaires and local survey methods parallel to those used in national surveys.

Producing notable improvements in the monitoring of birth defects will be a more costly proposition. The Environmental Protection Agency can, however, take advantage of the current movement among the states of the U.S. to develop birth defect monitoring systems of their own. The panel recommends that EPA

adopt a long-run strategy for improving birth defects monitoring through cooperative efforts with the states and other federal agencies. These efforts would involve:

- establishing a national clearinghouse and data improvement center on birth defects monitoring;
- providing matching funds to state health agencies to stimulate the expansion and upgrading of state-level monitoring systems;
- exploring the feasibility of a jointly-funded network of birth hospitals that would provide high-quality continuing data on malformations in a representative sample of U.S. births.

Finally, the panel urges EPA to provide support for basic research aimed at improving the scientific capability to demonstrate causal connections between environmental contamination and reproductive disorders.

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COMPOSITION OF THE WORKING GROUP

The members of the Working Group on Human Reproductive Outcomes were:

Lewis Holmes, M.D., Massachusetts General Hospital. Dr. Holmes is a specialist in newborn surveillance and congenital malformations.

Neil A. Holtzman, M.D., M.P.H., Health Program, Office of Technology Assessment. Dr. Holtzman's focus is genetics. Furthermore, he was instrumental in setting up the Maryland Birth Defects Reporting and Information Service.

Casey Jason, M.D., is a practicing physician in northern Virginia with particular expertise on the issue of early miscarriage.

Graham Kalton, Ph.D., Survey Research Center, University of Michigan. Dr. Kalton is well known for his work in survey sampling and statistics.

Donald Mattison, M.D., University of Arkansas School of Medicine. Dr. Mattison's research areas include reproductive toxicology and obstetrics.

Dorothy Warburton, Ph.D., Columbia University. Dr. Warburton is a human geneticist whose major research interests are cytogenetics and the etiology of embryonic and fetal death.

Janice Bakewell, from the Missouri Center for Health Statistics, represented a state that has developed an ongoing system for birth defects monitoring.

Federal Agency Representatives

The following individuals represented their federal agencies at the Working Group meetings. Their participation in the Working Group should not be interpreted as agency endorsement of the findings and recommendations made in this report.

William Pratt, Ph.D, and William D. Mosher, Ph.D, National Survey of Family Growth, National Center for Health Statistics;

Melissa Adams, Ph.D., Birth Defects Branch, Centers for Disease Control;

Michael Gruber, Ph.D., Susan Perlin, and Sherry Selevan, Ph.D., Environmental Protection Agency;

Woodie Kessel, M.D., Division of Maternal and Child Health, BHCDA, HRSA, U.S. Public Health Service;

Pat Shiono, Ph.D., National Institute of Child Health and Human Development;

Clara G. Schiffer, Department of Health and Human Services;

Robert L. Heuser and Stephanie Ventura, Natality Statistics Branch, National Center for Health Statistics;

Peter Gergen, M.D., Division of Health Examination Statistics, National Center for Health Statistics.

Child Trends' staff also wishes to thank Delbert Dayton, M.D., of the National Institute of Child Health and Human Development and Allen Wilcox, Ph.D. of the National Institute of Environmental Health Sciences, who did not attend the meetings, but provided valuable assistance.

Child Trends Staff

The following members of the Child Trends' staff took part in the Working Group meetings and helped to draft this report:

Christine Winquist Nord
Nicholas Zill, Ph.D.
Kristin A. Moore, Ph.D.

Further information on the operation of current data systems, the deliberations of the Working Group, and the reasoning behind the findings and recommendations reported herein may be found in the Background Report that accompanies this document.