

**Birth Defects Registry**  
Division of Genomics, Perinatal Health and Chronic Disease Epidemiology  
Bureau of Epidemiology  
Michigan Department of Community Health  
Revised September 2004

***What are Birth Defects?***

Birth defects are abnormalities that occur while the fetus is developing and affects approximately 3% of births. The leading cause of infant mortality within the first year of life is due to birth defects, which account for over 20% of deaths. The majority of them occur during the 1<sup>st</sup> trimester of pregnancy due to genetics or environmental exposures, however 60-70% have unknown etiology. All women are susceptible to having a child with a birth defect, regardless of age, race/ethnicity, education, and income levels. Birth defects can be grouped into structural/metabolic abnormalities (e.g. heart defects, PKU), congenital infections (e.g. rubella), and other causes (e.g. FAS).

***Why Study Birth Defect Clusters?***

Cluster studies help identify potential environmental exposures that can lead to birth defects and alleviate any community concern about birth defects and possible causes. If a teratogen is identified in a cluster investigation, it can be removed or avoided, decreasing the risk for birth defects. However, a majority of clusters happen due to normal chance deviations over time. Other clusters may be due to changes in diagnostic procedures or hospital referral patterns. Infrequently, clusters occur because of environmental exposures shared by all of the parents. Three common attributes of clusters are 1) a large excess of the same birth defect 2) the same possible biological exposure of all cases and 3) a characteristic pattern. Also, if an association exists and the rate of birth defects is ten times the normal, then an association can be detected.

***Responding to Birth Defect Concerns***

The Division of Epidemiology Services, Michigan Department of Community Health (MDCH) responds to calls, letters, and e-mails from citizens, workers, union representatives, and employers who are concerned about birth defect cases that are potentially occurring more often than expected (clusters), or are believed to be associated with environmental exposures in their communities and/or work places.

As used in this protocol, the term “birth defect cluster” is an unusual aggregation, real or perceived, of birth defect cases that are grouped together in time and space, that are reported to a health agency.

## Stage 1: Initial Contact, Response, and Evaluation

*Purpose: Collect information about the birth defect(s) from the reporting person(s).*

- A. Gather initial information using the Cluster Information Request Sheet (Appendix A) as a guide
- Type(s) of birth defect
  - Number of cases
  - Geographic area of concern
  - Time period of concern
  - Usual number of cases seen

- B. Discuss initial impression with the informant.

- Birth defects are more common than most people realize (approximately 1 in 33 or 3% of births).
- It is very difficult to link environmental exposure to a birth defect.
- A variety of birth defects in a cluster argue against any common linkage.
- Conditions that look similar may be due to different processes (such as structural deformities). Others may appear clinically different but related developmentally (for example neural tube defects).
- Common rates of birth defects (Centers for Disease Control and Prevention)

Congenital Heart Defects	1:100 to 1:200
Oral Clefts	1:700 to 1:1000
Down's Syndrome	1:800
Neural Tube Defects	1:1000

- C. Closing the conversation with the informant.

- Assure the informant that he or she will receive a written response.
- Clarify what the informant wants.
- Ask the informant if they want more information sent to them about the birth defect(s) in question.
- Get identifying information about the informant (name and phone number).
- Ask how the informant learned of the cluster.
- Give the informant your name and phone number.

\*If informant needs to obtain more information, wait until all information is received before beginning the investigation. If there is no response within 6 months, tell the informant that the cluster investigation will be closed if more information is not sent to MDCH.

- D. Following the conversation with the informant, contact the local health department and other appropriate personnel to determine whether to close the case or investigate it further.

- Continue investigation if
  - ♦ There are at least 3 cases of the same or developmentally same birth defect.

- ♦ Can verify the cases.
  - ♦ There is a potential environmental exposure.
  - Discontinue investigation if the cluster does not meet any of these requirements and prepare a summary report to be distributed to the concerned citizen, other interest groups, and the appropriate local health department.
- E. Maintain a log throughout the investigation of all contacts and include date, time, informant identification, birth defect, exposure, and geographic area. Any follow-ups should be logged. Personal health information is confidential. To protect patient privacy, all e-mail communications should not include any personal identifiers.

## **Stage 2: Assessment**

### ***I. Preliminary Evaluation***

*Purpose: Provide an estimate of the likelihood that a statistically significant excess has occurred.*

- A. Gather information about the birth defect, common risk factors, and background rates.
- B. Develop a case definition and that includes the following:
- Geographic area of delivery
  - The time period when the cases occurred
  - The birth defect of interest
- C. Data Analysis
- Determine the number of live-births in target geographic area and time period based on the information provided by the initial contact (using the information from the Cluster Information Request sheet).
  - Calculate the observed and expected rates (per 10,000).
  - Use a reference rate, such as the Michigan or National rate for comparison.
  - Determine if there is a statistically significant increase between the observed and the expected rate using confidence intervals or the Cluster Software version 3.1.
- D. Evaluation
- Continue the investigation if:
    - ♦ There is a statistically significant increase in birth defects AND/OR
    - ♦ The rate in the target area is higher than expected rate although not statistically significant
  - Discontinue investigation if it does not meet these requirements.
    - ♦ Prepare a summary report to be distributed to the concerned citizen, other interest groups, and the appropriate local health department.
    - ♦ Note in log that the cluster investigation is being closed.

## ***II. Occurrence/Exposure Evaluation***

*Purpose: Ascertain all cases within the defined geographic area and time period; Design and perform a thorough investigation; Evaluate information concerning potential exposure.*

- A. Verify the diagnosis through various sources, such as the Michigan Birth Defects Registry (MBDR). If the time period is outside of coverage for the MBDR, other data sources include, doctor, vital records, health care facilities, and service agencies.
- B. Determine the number of live births in the surrounding geographic area and time period that correspond with the case definition.
  - All birth defects in child/fetus
  - Date of delivery
  - Gestational age
- C. Obtain the following information from the data source(s), using the Cluster Questionnaire (Appendix B):
  - a. Case name
  - b. Geographic area of residence at delivery
  - c. Potential exposure(s)
  - d. Maternal and paternal age
  - e. Maternal and paternal race (Optional)
- D. Tabulate all cases of the birth defect (include both cases found in this step and initial cases).
- E. Check a list of birth defect diagnoses by case to see if there is any pattern of defects occurring within children or fetuses.
- F. Form a team to work on cluster (if necessary). Designate 1-2 people to whom questions should be directed.
- G. Data Analysis
  - Calculate the observed rate and expected rate for surrounding area (cases per 10,000).
  - Use a reference rate, such as the Michigan or National rate for the specific birth defect.
  - Determine if there is a statistically significant increase between the observed and expected rates for the surrounding area ( $p < 0.05$ ).
  - Determine if the target area has a significantly higher observed rate compared to the surrounding area and explore further the potential association with an exposure
  - Assess the likelihood that an event-exposure relationship occurred (help may be needed from the Department of Environmental Quality-DEQ).
  - Control for any potential confounders such as maternal age or race

- H. Assess the community perceptions, reactions, and needs (help from DEO, if necessary).
- I. Evaluate the need for gathering and analysis of environmental monitoring data and possible recommendations.
- J. Prepare a report combining the epidemiologic information with the environmental information.
  - a. Include description of methods used to find and verify cases as well as the statistical analysis.
  - b. Describe any statistically significant excesses.
  - c. Address any specific environmental concerns.

**The following steps will require and thus be conducted with IRB approval for research study.**

### **Stage 3: Major Feasibility Study**

*Purpose: Determine if it is possible to perform an epidemiological study linking the birth defect and the potential exposure.*

- A. Perform detailed literature review of epidemiological and biological plausibility about the potential relationship between exposure and birth defects.
- B. Consider the appropriate study design, including costs and expected outcome of each study design.
- C. Determine what data should be collected about the cases and controls.
- D. Determine the nature, extent, and frequency of birth defects and the methods used for environmental (exposure) measurements (if needed). Do this in conjunction with the appropriate state/federal agency.
- E. Describe the logistics of data collection and processing.
- F. Determine the appropriate analysis plan, including the hypothesis to be tested and necessary power to detect differences. Assess the epidemiologic and policy implications of various potential results.
- G. Assess the current social and political environment, considering the impact of decision and outcomes. Reassess the community perceptions/reactions/needs.
- H. Assess whether there is adequate resources to conduct the study. Estimate the consequences of various potential findings on staff, financial resources, and the community affected.

- I. Write a report summarizing feasibility study and communicate to the appropriate persons.
- J. If study suggests etiologic investigation is warranted, proceed to Stage 4.

**Stage 4: Etiologic Investigation**

*Purpose: To perform an etiologic investigation of a potential birth defect-exposure relationship.*

- A. Using the major feasibility study as a guide, develop a protocol.
- B. Implement the study.
- C. Write report and communicate findings to the appropriate persons.

Not for Distribution

## **Appendixes**

**Appendix A**

**CLUSTER INFORMATION REQUEST: Cluster Summary**

**Michigan Department of Community Health**

Division of Genomics, Perinatal Health and Chronic Disease Epidemiology

Bureau of Epidemiology

201 Townsend St

Lansing, MI 48909

**SUMMARY OF POSSIBLE CLUSTER:**

Birth Defects of concern:

- 1.
- 2.
- 3.
- 4.
- 5.

Residence of mothers when the children were born:

Time period of cases:

Do you have any information on the usual numbers of cases seen? If so, please describe.

How did you become aware of the birth defect cluster?

What do the parents' have in common?

Who else can I contact for more information about the cluster? Have you discussed concerns with the local health department?

**Appendix B**

**Cluster Questionnaire**

**Michigan Department of Community Health**

Division of Genomics, Perinatal Health and Chronic Disease Epidemiology

Bureau of Epidemiology

Lansing, MI 48909

**Information on Child**

Name of Child: \_\_\_\_\_ Sex: \_\_\_\_\_

Birth date of Child: \_\_\_\_\_ Race: \_\_\_\_\_

Current Residence of child: \_\_\_\_\_

County of Residence at delivery: \_\_\_\_\_

Hospital of delivery: \_\_\_\_\_

What birth defect(s) does he/she have? Please describe in as much detail as possible.

\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_  
\_\_\_\_\_

Time diagnosed with birth defect: \_\_\_\_\_

Where: \_\_\_\_\_

**Information on Mother**

Age of mother at time of delivery: \_\_\_\_\_ Race of mother: \_\_\_\_\_

Residence of mother at delivery: \_\_\_\_\_

Was there a previous (or additional) affected pregnancy with the same birth defect? \_\_\_\_\_

Any significant medical conditions, such as diabetes, thyroid disease, seizure disorders, or infections, at the time of pregnancy? \_\_\_\_\_

Any medication taken during delivery: (Y/N)  
What are they? \_\_\_\_\_

Any reproductive assisted techniques used for this pregnancy: (Y/N)  
What procedures: \_\_\_\_\_

Any fertility medications taken for this pregnancy: (Y/N)  
What are they? \_\_\_\_\_

**Information on Father**

Age of father at time of delivery: \_\_\_\_\_

Race of father: \_\_\_\_\_

**Risk Factor Assessment**

Do you have any environmental or health concerns about the area? If yes, please describe.

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Is there a positive family history of birth defects/syndromes/mental retardation? If yes, please describe.

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Please describe the occupation of both parents/guardians (if possible) just prior to and during the pregnancy. Include any possible occupational exposures to agents such as chemicals, heavy metals, or radiation.

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**This protocol borrows heavily from the following:**

Centers for Disease Control and Prevention. “Guidelines for Investigating Clusters of Health Events”. MMWR, July 27, 1990 / Vol. 39 No. RR-11.

Centers for Disease Control and Prevention. “Birth Defects: Frequently Asked Questions (FAQs)”. Accessed on Sept. 22, 2004. Available at <http://www.cdc.gov/ncbddd/bd/faq1.htm>.

California Birth Defects Monitoring Programme, “Investigating Clusters of Birth Defects: Guidelines for a Systematic Approach”. 1999.

Texas Birth Defects Monitoring Division, “Birth Defect Cluster Investigation Protocol”. 1999.

Washington State Department of Health, “Guidelines for Investigating Clusters of Chronic Disease and Adverse Birth Outcomes”. 2001.

[www.modimes.org](http://www.modimes.org)

<http://www.cdc.gov/ncbddd/bd/default.htm>

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