National Birth Defects Prevention Study
OMB 0920-0010
Extension

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The National Birth Defects Prevention Study

A. Justification

A.1. Circumstances Making the Collection of Information Necessary

Adverse reproductive outcomes such as birth defects and genetic diseases are associated with substantial morbidity and mortality in the United States. Roughly three to four percent of all newborn babies are affected by some form of serious defect. Seventeen of the most clinically important types of birth defects cost this country approximately $6 billion in 1992 alone. Birth defects are the leading cause of infant mortality and the fifth leading cause of loss of potential years of life before age 65. One in five infant deaths is due to birth defects. Identifying the cause and subsequently controlling birth defects would help bring us closer to reducing infant mortality to 4.5 per 1,000 live births, a Healthy People 2010 objective.

However, to date primary preventive measures are available for only a few birth defects. For example, vaccination programs have reduced the incidence of congenital rubella syndrome, Rh hemolytic disease of the newborn can be prevented by appropriate medical practice, and genetic counseling can provide parents with information about the increased risk of Down Syndrome associated with advanced maternal age. And, perhaps most importantly, folic acid dietary supplements can theoretically prevent up to half of all cases of fatal or permanently disabling neural tube defects such as anencephaly and spina bifida.

For the vast majority of the remaining birth defects, the causes are simply not known, and cases continue to occur. The existence of this continuing burden justifies reasonable attempts to reduce birth defects and genetic diseases. The first step in understanding and controlling adverse health outcomes is always surveillance for those outcomes by public health agencies. The CDC initiated birth defects surveillance in 1967, in the wake of the thalidomide disaster, with the Metropolitan Atlanta Congenital Defects Program (MACDP). This surveillance system was meant to serve as a defense against unnecessary infant mortality and morbidity from teratogenic exposures. It was to be an early warning system for birth defect epidemics as well as the foundation upon which to do the epidemiological analysis needed to discover the cause of such epidemics. In order to achieve these ends, the MACDP has monitored (through medical record abstraction) the occurrence rates of various types of defects in the Atlanta population by recording every major congenital anomaly that has occurred among all children born in the Atlanta metropolitan area. MACDP has carried on this effort without a break since 1967, making it the longest running active surveillance system in the world.

Beginning in 1997, the State of Georgia exercised its option to require the reporting of birth defects under the state's disease reporting regulations, which list birth defects as a condition whose reporting is required by law. The Georgia Department of Community Health (DCH) authorized the CDC to serve as its agent in the collection of these case reports. (Authorization from the GA DCH is renewed on a yearly basis). **Attachment C** contains the authorization that will expire on 12/31/2013. MACDP findings are shared with the state. Since birth defects surveillance in Atlanta is now a state requirement, the CDC is no longer requesting OMB clearance for this activity. The Division of Birth Defects and Developmental Disabilities, however, is seeking a reinstatement without change of its OMB clearance for the additional data

collection that is carried out under the National Birth Defects Prevention Study (NBDPS) (CDC Protocol # 2087, Expiration 1/29/2013 **Attachment D**).

To improve its ability to determine the causes of birth defects, the CDC paired up the Birth Defect Risk Factor Surveillance study (BDRFS) with MACDP in 1993, following OMB approval. The BDRFS collected additional information on exposure and susceptibility factors for cases of birth defects and for comparison controls. To help reduce birth defects among U.S. babies, in 1996 Congress directed the CDC to establish the Centers of Excellence for Birth Defects Research and Prevention. This was formalized with passage of the Birth Defects Prevention Act of 1998 (see **Attachment A** for Public Law 105-168,). This Act authorized CDC to (1) collect, analyze, and make available data on birth defects; (2) operate regional centers that will conduct applied epidemiological research for the prevention of birth defects; and (3) provide the public with information on preventing birth defects. In 1996, CDC awarded cooperative agreements to 7 states (AR, CA, IA, MA, NJ, NY, and TX) to establish Centers for Birth Defects Research and Prevention (CBDRP). In September 2002, two additional states, UT and NC, were funded and NJ did not receive continuation funding. Therefore there are currently a total of nine participating sites (AR, CA, IA, MA, NC, NY, TX, UT and the DBDDD, CDC in Atlanta). See **Attachment D2** for current list of NBDPS centers. One of the main activities for each Center is to conduct the NBDPS in their state (see section A.4).

Infants with birth defects are identified through the birth defects surveillance system in each participating state, control infants are randomly selected from electronic birth certificates or birth hospitals in the same population, and mothers of case and control infants are interviewed by phone about their medical history, pregnancies, environmental exposures and lifestyle. Genetic samples are obtained through the collection of DNA from cheek cells. After completing the interview, participants are sent a packet in the mail and are asked to collect cheek cells from the mother, father, and infant using small brushes. The brushes containing cheek cells are then sent back to the lab by mail.

OMB approval (OMB 0920-0010) for NBDPS was originally obtained in September 1999 and will expire July 31, 2012. This request is for a 3-year Extension. Currently, OMB approval encompasses the data collected from all eight states (AR, CA, IA, MA, NC, NY, TX and UT) and by the DBDDD, CDC in Atlanta. These data include 400 planned interviews (300 cases and 100 controls) and an interview burden of approximately 400 hours per center per year. This current request, like the previous request in September 2009, will yield a maximum of 3,600 planned interviews, 2,700 cases and 900 controls. These interviews will result in a maximum interview time of 3,600 hours per year when accounting for all nine centers.

A1.1. Privacy Impact Assessment

A Privacy Impact Assessment was done previously for this project in 2004, and a Certificate of Confidentiality was signed by Dr. James Stephens (see Section A.10) on January 28, 2010 and will expire on at the end of January of 2014. We provide a PIA overview below.

Overview of the Data Collection System

The data will be collected by questionnaire using a computer assisted telephone interview (CATI). The average time to complete the interview is estimated to be one hour. The interview used in the NBDPS is designed to ascertain only questions that are pertinent and useful in identifying possible risk factors associated with adverse reproductive outcomes. The CATI makes it possible to complete the interview in segments so that participants have the option of completing the interview in several sessions rather than all at once. The CATI was approved by OMB in April, 2010 and is included in **Attachment E**.

Description of Information to be Collected

Using a computer assisted telephone interview (CATI) system, information in identifiable form (IIF) is collected, maintained and passed through the CDC database via a Secure Data Network (SDN) to facilitate the compilation of data for the CBDRP. The IIF is collected by collaborators and contractors and is securely transmitted to the CDC through the SDN. The following are all categories of IIF collected: name, data of birth of mother, father and baby, mailing address, phone numbers, email addresses, medical information and notes, biologic specimens, education records and employment status. Other categories of non-IIF data include pregnancy history (i.e. prenatal diagnosis, prenatal care and fertility), maternal conditions and illnesses (i.e. diabetes, high blood pressure and infections), family history, lifestyle and behavioral factors (i.e. stress, alcohol use, and substance abuse), nutrition, multivitamin use, environmental exposures, occupational history and family demographics (i.e. birth place and household income).

Identification of Website(s) and Website Content Directed at Children Under 13 Years of Age

A website for this project can be found at http://nbdps.org/. The NBDPS website is not nor will it ever be directed at children under13 years of age.

A.2. Purpose and Use of the Information Collection

How the Information will be Used and for What Purpose:

The purpose of the NBDPS is to evaluate factors associated with the occurrence of birth defects and to test hypotheses for gene-environment interactions involved in the etiology of birth defects. Information collected in the interview (**Attachment E**) provide data for the evaluation of suspected new teratogens, mutagens, or environmental agents that are not prevalent enough to cause epidemics. For example, the information on family history of birth defects is useful in assessing the degree to which subsequent children in a family are at risk of having a birth defect or adverse outcome. The data gathered on parental occupation is useful in assessing the impact of the work place on reproductive outcome. The interviews also offer the possibility of identifying protective factors such as diet or vitamin use. The DNA collected from the cheek cells will be used to study genetic susceptibility to the effects of environmental agents. Using a candidate gene approach, it is possible to evaluate the role of genetic differences at specific gene loci and their interaction with other genes or specific environmental exposures in the etiology of birth defects. Candidate genes are genes that, because of their function or position, are believed to play a role in the embryology and pathophysiology of different organ systems.

The NBDPS has and will continue to provide the nation with a continuing source of information on potential causes of birth defects and will serve as a mechanism for identifying new substances

in the environment that are harmful to fetal development. Over 100 manuscripts have already been published using NBDPS data (see Section A.16), and many more manuscripts are proposed and currently being written. The information NBDPS provides is critical to the mission of the Public Health Service to reduce morbidity and mortality due to congenital malformations. Data from the NBDPS and the earlier version, the BDRFS, also play an important role in the decision-making process that determine federal research agendas, birth defect prevention activities, and the direction of funding programs such as cooperative agreements.

Impact of Proposed Collection on the Respondent's Privacy:
Information in identifiable form (IIF) is collected for this study, but privacy of the respondent is protected as detailed in section A.11. Because of these precautions, no impact on the respondent's privacy is anticipated as a result of participation in NBDPS data collection.

A.3. Use of Improved Information Technology and Burden Reduction

Questionnaire
The questionnaire is administered as a computer assisted telephone interview (CATI). The average time to complete the interview is approximately one hour. The interview used in the NBDPS is designed to ascertain only questions that are pertinent and useful in identifying possible risk factors associated with adverse reproductive outcomes. The CATI makes it possible to complete the interview in segments so that participants have the option of completing the interview in several sessions rather than all at once. The CATI was pilot tested with new mothers to ensure that the questions obtained the desired information and were sensitive to the circumstance surrounding the birth of a baby with a birth defect. When the study was changed from the BDRFS to the NBDPS, an expert panel reviewed the questionnaire. Questions that did not appear to be yielding complete and accurate information were dropped or revised. Topics that provided very little data for analysis were also dropped. Studies have suggested that diet, particularly vitamins and minerals, may be associated with specific birth defects. In place of the questions that were dropped, food frequency questions were added to the questionnaire in March 1999. The food frequency items that were added to the questionnaire are validated and used in many other studies (Willett W. Nutritional Epidemiology, In: Monographs in Epidemiology and Biostatistics, Oxford University Press, New York, 1990). Also, an association between water disinfection byproducts and birth defects has been suggested. The existing questions dealing with tap water exposure were expanded in February of 2000. The entire questionnaire was evaluated again in 2002-2003. Questions that did not yield complete and accurate information or provided very little data were dropped. Recent additional changes to the questionnaire include three centers, MA, GA and TX, dropping the food frequency questions on November 1, 2011 in an attempt to increase participation/completion rates by shortening the interview. In addition, physical activity questions based on the International Physical Activity Questionnaire (IPAQ) were added in April of 2010. These questions provide new information about the prevalence of periconceptional physical activity and association of physical activity and major birth defects. The modified CATI was approved by OMB in April, 2010 and is included in **Attachment E**.

The NBDPS is being conducted at nine locations around the country. To facilitate the compilation of the data, the interview data is sent to CDC via the Secure Data Network (SDN) using a replication feature developed in-house. The replication process enables the

data to be transferred to the central storage database at the same time that the CATI program is updated. Whenever program corrections are made to the CATI, each site receives those changes when they replicate their data. This way, all of the sites are kept standardized.

A.4. Efforts to Identify Duplication and Use of Similar Information

Efforts to identify duplication include periodic systematic reviews of the scientific literature and frequent discussions with birth defects researchers at federal agencies and research institutions across the United States as facilitated by Center and CDC contacts. The NBDPS is the only case-control study of the 30 selected birth defects (see **Attachment F for a list of birth defects studied in the NBDPS**) being conducted in the U.S. at this time.

The NBDPS is being conducted by the Centers for Birth Defects Research and Prevention (CBDRP) in eight states (AR, CA, IA, MA, NC, NY, TX and UT) and by the DBDDD, CDC in Atlanta. All of the Centers are using the same processes for identifying eligible cases and controls, participant contact, data collection, and data processing. Collaboration among these Centers and CDC is essential for the success of the NBDPS because it allows scientists with differing expertise to work together, substantially improving the ability to better understand birth defect risk factors. Because birth defects are rare, it takes many years to accumulate enough cases of a particular defect to have the power to study risk factors for that defect. This collaborative effort will enable researchers to study the epidemiology of some rare birth defects for the first time. It may also enable researchers to identify rare exposures, such as genetic variations, that are associated with the more common birth defects.

A.5. Impact on Small Businesses or Other Small Entities

No small businesses are or will be involved in this study.

A.6. Consequences of Collecting the Information Less Frequently

For the NBDPS, the mothers of the cases and controls are contacted for a telephone interview and are then sent kits for the collection of cheek cells in the mail. Very rarely a mother may have to be re-contacted if during the quality control process, some information was not clear in her interview or if the cheek cell specimens need to be re-sampled due to lack of DNA or contamination. Otherwise, this is considered a one-time survey.
There are no legal obstacles to reduce the burden.

A.7. Special Circumstances Relating to the Guidelines of 5 CFR 1320.5

The project fully complies with all of the guidelines of 5 CFR 1320.5.

A.8. Comments in Response to the Federal Register Notice and Efforts to Consult Outside the Agency

A.8A. 60-Day Federal Register Notice

The 60-day notice was published in the *Federal Register, Vol. 77, No. 36, pp. 10750-10751,* on February 23, 2012 (**Attachment B**). There were no public comments.

A.8B. Consultation Outside the agency

The principal investigators at each CBDRP work collaboratively with CDC scientists on scientific aspects of study design and analysis, including development of the study protocol, interview instrument design, and study conduct. Committees were formed with representatives from each CBDRP to design the collaborative case-control study. The **standards committee** designed the protocol for the study including standard forms and procedures for identifying, contacting, and interviewing study participants. The **questionnaire and methods committee** revised the BDRFS mother interview instrument and arranged to have the questionnaire placed into a CATI format. The questionnaire committee also evaluates the interview instrument. The **clinicians committee** (geneticists and clinicians from each CBDRP) decided on the case definitions for the 30 birth defects included in the study and developed guidelines to assist with case identification and review, medical record abstraction, and coding. The **biologic committee** designed the protocol for the collection of biologic samples and developed a plan for banking, sharing the biologic specimens, and is responsible for the ongoing quality control analysis of the biologic samples and the recommendation of genes for study. The **data sharing committee** has the ongoing task of deciding how the data will be equitably shared for analysis purposes. This committee is responsible for review of all protocols for data analysis as well as addressing human subjects' issues, data access, collaboration, and authorship. The scientists involved in the NBDPS represent the greatest concentration of expertise and experience on birth defects in the United States (please see **Attachment G** for a detailed list of collaborators).There have been no major problems identified through these consultations.

A.9. Explanation of Any Payment or Gift to Respondents

Research suggests that remuneration results in increased response rates and indicates to respondents that the investigators believe their time is valuable. Remuneration may also help prevent biases introduced by lower participation rates among the economically disadvantaged. Literature examining the benefit of remuneration was summarized by Yu (Yu J, et al. A quantitative review of research design effects on response rates to questionnaires. J Marketing Res 1983;20:36-44). It reviewed 497 response rates found in 93 journal articles and found that response rates increased with monetary and non-monetary incentives.

The NBDPS began remunerating participants for the maternal interview in January 2000. A $20 money order is mailed in the introductory interview packet. Since the $20 money order was added, participation rates for both cases and controls initially increased then stabilized between approximately 60 and 70%.

The NBDPS also remunerates participants for the biologic sample collection portion of the study. The cheek cell kits include $20 as an incentive to complete them and send them back. Overall, approximately 60% of participants completing the interview send in a completed cheek cell kit. While some subjects have stated that they do not wish to provide cheek cell samples due to their concerns about genetic testing, many subjects state that it is time consuming and difficult to remember to complete the kit and mail it back. In June of 2002, we added an additional $20 incentive in two sites (New York and Atlanta) that was linked to the return of the cheek cell kits as a pilot study. Currently, all Centers implement a total of $60 (three $20 incentives) for subjects who choose to complete the entire study including the return of the cheek cell samples. The third $20 money order is provided to any mother who returned samples for herself and the

baby or for just herself if the baby is deceased. While samples are requested from the father, the third incentive is not dependent on the cooperation of the father since this may pose a hardship to those mothers who are not in regular contact with the father.

Given the time and inconvenience required for the entire study (interview and biologics), a total of $60 is an appropriate level of compensation. The additional $20 money order has increased the number of kits that are completed and returned to the Atlanta Center, particularly among non-White women (Crider et al. submitted to *Epidemiology*, December 2005). Among Black, Non-Hispanic women cheek cell participation increased from 31.7% to 46.0%. In the logistic model, the additional $20 money order was the only significant factor associated with increased participation among Black, Non-Hispanic women [OR=1.82, (95% CI, 1.22-2.78)]. Among Hispanic women, cheek cell participation increased from 36.6 to 45.6%. The third $20 money order, along with maternal education greater than 12 years and interview conducted in English were significant factors associated with cheek cell participation [OR 1.96(1.03-3.72), OR 2.14(1.13-4.07) and OR 3.00(1.56-5.78) respectively]. Although cheek cell participation among White, Non-Hispanic women increased from 60.7% to 62.7% upon implementation of the third $20 money order, this increase was not significant. Based on this research, all collaborating centers incorporated and currently use the three $20 incentive protocol.

A.10. Assurance of Confidentiality Provided to the Respondents

The Privacy Act Officer reviewed this OMB application and has determined that the Privacy Act is applicable. A contractor is used by NCBDDD to conduct interviews for the Atlanta site. Full names of respondents must be collected to enable the study purposes to be achieved. Records will be covered under the CDC Privacy Act system of records 09-20-0136, Epidemiologic Studies and Surveillance of Disease Problems. The NBDPS is based on the previous experience of the BDRFS, which was initiated at CDC and had 308(d) confidentiality assurance protection. The BDRFS was expanded in 1997 through cooperative agreements. The activities of the NBDPS project are both intramural and extramural, consisting of one CDC operated site in Atlanta, Georgia, and eight CDC-funded cooperative agreements in eight other states. Because all sites (except the CDC's Atlanta site) were funded by cooperative agreements and protection was needed for data at each site, it was determined by the CDC Office of General Counsel and the CDC Confidentiality Officer that a 301(d) Certificate of Confidentiality was the appropriate confidentiality protection. NBDPS received a Certificate of Confidentiality for the eight original study sites in August 1999, and the latest renewal was signed January 2010 (**Attachment H,** expiration September 2014).

The Certificate of Confidentiality, by preventing study staff from being forced under a court order or other legal action to identify study participants or provide individually identified data, supplies additional assurance to both participants and CDC’s cooperating researchers that the data collected will be kept confidential and will not be subject to potential release from a wide variety of sources. Because the topics of the study are sensitive, respondents are more likely to participate since they are assured their identity is secure and will not be subject to review by people outside of the research process (See interview telephone consent script and cheek cell collection written informed consent in **Attachments I and J** respectively).

The data to be covered by 301(d) confidentiality certificate protection include the interviews, clinical data, and results of testing on biological samples collected for the NBDPS. Each site operates a state surveillance program established by law that was operational prior to the Centers study. Surveillance data already in the possession of the sites is not to be included under the certificate. The data are properly safeguarded. Hard copy documents are kept in locked file cabinets. Computer databases are password protected. Data are transferred via the Secure Data Network. Access to individually identified study information is limited to a very small number of authorized study personnel. All personnel with access to study data must sign the NBDPS Confidentiality and Data Use Oath (**Attachment K**).

IRB Approval

CDC IRB approval for the NBDPS study is renewed yearly; current approval expires January 29, 2013 (See **Attachment D** for current CDC IRB approval letter).

A.11. Justification for Sensitive Questions

The maternal interview for the NBDPS asks questions about topics that may be considered sensitive: alcohol and drug use, history of sexually transmitted diseases, use of contraceptives, use of fertility medications and procedures, and household income. These topics are included in the study because several reports have linked these factors to birth defects, and these associations need further clarification. The interviewers are trained to emphasize not only the voluntary nature of the entire interview but the respondent's prerogative to not answer specific questions. There are four places before the interview takes place where the mother is informed that her participation is voluntary: the introductory letter, the question and answer pamphlet, the informed consent telephone script that is read to the mother before the interview, and the Human Subjects Fact Sheet.

The initial mailing to mothers about the study includes a pamphlet of questions and answers that includes the following: "*What if I don't want to answer*? You may skip any questions you wish." (see pamphlet, **Attachment L**)

There is also a statement in the introductory letter that reads: "Any information that could identify you will be kept private." (see introductory letter, **Attachment M**).

The Human Subject Fact Sheet informs participants of the following (**Attachment N**):

"As a potential participant in this research study, you have the right to:

- Be informed of the nature and purpose of the study.
- Be given an explanation of the procedures to be followed in the study.
- Be given a description of any discomforts and risks reasonably to be expected from the study procedures.
- Be given an explanation of any benefits you can reasonably expect from participation.

- Be informed of medical treatment, if any, available to you during and after the study if complications should arise.

- Be given an opportunity to ask any questions concerning the study or procedures involved.

- Be informed that you may withdraw from the study at any time without penalty.

- Be given the opportunity to decide to participate or not without the use of any force or undue influence on your decision.

All information that we gather in this study will be kept private. This is because the study has been given a Certificate of Confidentiality by the Centers for Disease Control and Prevention. This means anything you tell us will not have to be given out to anyone, even if a court orders us to do so, unless you say it's okay. We may share information about you with other researchers but that information will not identify you or anyone else in the study.

The National Birth Defects Prevention Study Question and Answer brochure will give you more information about how your privacy is protected in this study.

If you have questions about your rights as a subject in this research study, please call the Office of the Deputy Associate Director for Science for CDC at 1-800-584-8814, leave a message including your name, phone number, and refer to protocol #2087, and someone will call you back as soon as possible."

The informed consent telephone script (**Attachment I**) also informs the mother that there are some questions about sensitive issues in the interview and that she can choose not to answer any specific questions. The script also emphasizes that the mother's answers are confidential and that her identity will remain private.

The collection of the cheek cells from the mother, father and infant requires written informed consent (**Attachment J**). Again the participants are reminded that all parts of the study are voluntary and all data gathered in the study are stored without names or personal identifiers. The protection afforded by the Certificate of Confidentiality is explained again in the written consent.

The interview data from the NBDPS is compiled on a server at CDC. After the cheek cell samples have been collected, each CBDRP retains at their site, one brush. The other brush is sent to the CDC Centralized Laboratory for processing. Once processing is complete at the Centralized Laboratory, samples are sent to a centralized storage facility where they will be stored and identified only by study ID number. The compiled interview data and biologic material do not contain any personal identifiers. The interview data is kept on a password-protected computer in a locked office. The biologic material is stored in rooms that are secured by cardkey access. The physical facilities for both the interview data and biologic material have restricted access with 24-hour security guards.

A.12. Estimates of Annualized Burden Hours and Costs

The interview is estimated to take approximately 64 minutes. The interview is titled "National Birth Defects Prevention Study: Mother Questionnaire, CATI Version 5.1, April 6, 2010" (see **Attachment E**). Using the one hour estimate, a maximum of thirty-six hundred interviews are planned annually, 2,700 case mothers and 900 control mothers, resulting in a maximum interview burden of 3,640 hours for all Centers per year over three years. The one hour burden includes the time for the telephone consent script (**Attachment I**) which is reviewed with the mother at the beginning of the call to collect the information via the CATI interview.

The collection of cheek cells for Biological Specimen Collection from the mother, father, and infant is estimated to take about 10 minutes per person. Each person will be asked to rub 1 brush inside the left cheek and 1 brush inside the right cheek for a total of 2 brushes per person. Collection of the cheek cells takes approximately 1-2 minutes, but the estimate of burden is 10 minutes to account for reading and understanding the written consent form and specimen collection instructions and mailing back the completed kits. The anticipated maximum burden for collection of the cheek cells is 600 hours for the mothers, fathers and infants each, resulting in a total burden of 1,800 hours per year over three years. The total annual burden hours for all activities for all individuals for all Centers is 5,440 hours.

Table A.12-1 **Estimates of Annualized Burden Hours**

Respondents	Form Name	Number of Respondents	Number of responses per respondent	Avg. burden per response (In hours)	Total Burden Hours
Mothers (interview)	1. NBDPS mother questionnaire (CATI V 5.1 (Attachment E); 2. Telephone script (Attach I)	3,600 (mothers)	1	64/60	3,640
Mothers, fathers, infants (cheek swabs)	1. letter to families (Attach P) 2. written informed consent for cheek cell collection (Attach J) 3. instructions for collecting cheek cells (Attach Q)	10,800 (mothers + fathers + infants)	1	10/60	1,800
TOTAL					5,440

Table A.12-2 **Estimated Annualized Burden Costs**

Type of Respondents	No. of Respondents	No. Reponses per Respondent	Avg. Burden per Response (in hours)	Total Burden Hours	*Hourly Wage Rate	Total Respondent Costs
Mothers (interview)	3,600	1	64/60	3,640	$10.00	$36,400
Mothers (cheek swabs)	3,600	1	10/60	600	$10.00	$ 6,000
Infants (cheek swab done by mother	3,600	1	10/60	600	$10.00	$ 6,000
Fathers (cheek swabs)	3,600	1	10/60	600	$10.00	$ 6,000
TOTAL						$54,400

***Approximately 75% of women of child-bearing age do participate in the U.S. workforce (see http://www.bls.gov/opub/ted/2000/feb/wk3/art03.htm). A subset of these child-bearing women are part-time and not full-time workers. We have used the National Compensation Survey to aid in our calculation of the hourly wage rate for our table entitled "Estimated Annualized Burden Costs" (please see the U.S. Department of Labor publication entitled: "National Compensation Survey: Occupational Wages in the United States, June 2006" located at http://www.bls.gov/ncs/ocs/sp/ncbl0910.pdf). We have thus calculated an hourly wage rate of $10.00 for the respondents for this ICR.**

Interview costs: A respondent mother can have time costs for the interview or biological specimen collection. A respondent father and infant can have time costs for the biologic specimen collection only. An interview is estimated to take 64 minutes and is estimated to cost $10. A maximum of thirty-six hundred interviews are planned, 2,700 cases and 900 controls, resulting in a maximum interview burden of 3,640 hours for all Centers per year over 3 years ($36,400 per year).

Specimen costs: The anticipated maximum burden for collection of the cheek cells is 1,800 hours per year over 3 years. Since one of the parents will have to collect the cheek cells from the infant, the hourly wage rate was applied to the infant's time burden so the total burden for the biologic specimen collection will be $6,000 per year.

A.13. Estimates of Other Total Annual Cost Burden to Respondents or Recordkeepers

There are neither (a) total capital and start-up costs, nor (b) operation, maintenance, and purchase of services costs for respondents or record keepers resulting from the collection of information.

A.14. Annualized Costs to the Federal Government

See Table A.14-1 for a total annual cost estimate for one year to conduct the entire study of the NBDPS The current NBDPS activities under Funding Opportunity Announcement #CDC-RFA-DD09-001 began on December 1, 2008 and will end on November 30, 2013. We plan to continue activities after November 2013 under a new funding opportunity announcement to be published in FY 2013. It is anticipated that costs in future years will be comparable to those

shown in the table with appropriate adjustments for budget changes, inflation, and salary increases.

Table A.14-1: **Estimates of Annual Cost to the Government**

CDC and Contract Personnel*	**FTEs**	**Costs* (dollars)**
Epidemiologist, GS-15	.7	119,000
Epidemiologist, GS-13	.8	107,200
Epidemiologist, GS-14	.5	70,000
Medical Officer, GS-14	.25	38,000
Health Scientist, GS-14	.9	120,400
Medical Officer, GS-14	.5	91,200
Data Collection Supv, GS-13	1	132,000
Project Coordinator, GS-12	1	100,000
Programmer (contractor)	1	163,000
Programmer Q&A (contractor)	.9	105,300
Data Manager (contractor)	1	100,000
Data Manager (contractor)	.8	80,000
Lab Project Coordinator (contractor)	.5	110,000
Microbiologist GS–15	.25	42,000
Lab Technicians (contractor)	3	340,000
Laboratory supplies		120,000
Incentives for cheek cell collection		35,000
Cheek cell kits		10,000
Printing		10,000
Postage		5,000
Office Supplies		5,000
Travel		20,000
Equipment		6,000
Interview and coding contract		500,000
TOTAL COSTS		**$2,429,100**

*CDC personnel cost includes salary, benefits and physicians pay (if applicable). Contractor costs include direct and indirect cost plus profit are fully burdened.

A.15. <u>Explanation for Program Changes or Adjustments</u>

The estimated burden for this study has not changed since the last OMB approval.

A.16. <u>Plans for tabulation and Publication and Project Time Schedule</u>

Data from the BDRFS are currently being analyzed. Data collection for the NBDPS is ongoing and will continue for at least 3 more years. The first coded and cleaned dataset was released to the study Centers in October 2002. Enough interviews have been completed for several birth

defects to conduct analyses. Over 100 manuscripts have been written using NBDPS data, and nearly 300 additional projects have been proposed or begun analyses using NBDPS data.

For the purposes of analysis, individual defects will be categorized into appropriately homogeneous groups, including the presence of single and multiple defects. Analysis of risks from a given exposure will be carried out within broad categories, such as all vascular disruption defects, and be narrowed to a given defect such as gastroschisis.

Because controls are population-based and randomly selected, all controls can be utilized for any of the subgroup analyses which involve interview information. Additionally, other cases can be compared with the case group of interest in certain analyses, when appropriate.

The major analytic tool will be unconditional logistic regression. Relative risk estimates will first be made without consideration of potentially confounding variables. Important covariables such as maternal age and education will then be included.

An important analytic tool will be to look for evidence of gene-environment interaction in the analysis. Genetic information will be obtained using DNA-based polymorphisms. Individuals will be classified according to the presence or absence of specific susceptibility alleles, as well as whether they have those alleles in single (heterozygotes) or double dose (homozygotes). Evidence for interaction will be sought in logistic regression modeling using specific interaction terms. Detectable relative risks using all controls have been calculated based on population exposure frequencies of 10% and 20%, with power (beta) set at 0.80 and significance level (alpha) set at 0.05. For the larger defect categories, after 1 year, detectable relative risks range between 2.7 and 3.9. However, for the rarer defects, detectable relative risks are quite high until 5-year data have accumulated.

The findings published from this study have and will continue to be published in medical journals and presented at scientific meetings. Information that may be useful in preventing birth defects will be adapted for health education materials. 132 manuscripts utilizing NBDPS pooled data and over 200 abstracts have been published to-date (**Attachment O)**.

Table A.16-1 Project Time ScheduleError! Bookmark not defined.

Activity	**Time Schedule**
Data collection maternal interviews	1998 - Ongoing
Data collection cheek cells	1999 – Ongoing
Database coding	2000 - Ongoing
Analysis	Ongoing
Publication	July 2000 - beyond end of study

A.17. Reason(s) Display of OMB Expiration Date is Inappropriate

Expiration dates are displayed, so no exemption is sought.

A.18. Exceptions to Certification for Paperwork Reduction Act Submissions

No exceptions are sought.