Birth Defects Study To Evaluate Pregnancy exposureS (BD-STEPS)
OMB # 0920-0010

Supporting Statement B
Revision

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October 4, 2022

B. Collection of Information Employing Statistical Methods

B.1. Respondent Universe and Sampling Methods

Seven Centers for Birth Defects Research and Prevention (CBDRP) currently participate in BD-STEPS: Arkansas (AR), California (CA), Iowa (IA), Massachusetts (MA), North Carolina (NC), New York (NY), and CDC/NCBDDD's Division of Birth Defects and Infant Disorders (DBDID) serves as the site of record for Georgia (GA) . Cases for BD-STEPS in Atlanta are selected from the Metropolitan Atlanta Congenital Defects Program (MACDP) surveillance system, and cases for all other Centers are selected from established state surveillance systems. The collection of information for cases of selected birth defects does not employ statistical methods because all infants with one of the 22 birth defects are included (see **Attachment J**) in the state birth defects surveillance systems from which eligible cases are ascertained, and all cases with an eligible defect are included, not just a sample of cases. Individual birth defects are rare occurrences, so it is necessary to ascertain all cases in order to have enough cases of specific defects to study. Two Centers also collect information for all stillbirths without major defects (see **Attachment K**) in their respective study area. However, the controls in BD-STEPS are selected by a sampling process.

For BD-STEPS, each of the CBDRP will select randomly from the population (from either vital records or hospital birth logs) approximately 100 eligible controls each year for inclusion in the study. Whether hospital records or birth certificates are used as the source for control infants, the records are reviewed to ensure that, given the available information, the selected control-infant does not have a birth defect. Records are also reviewed to abstract information for the purpose of follow up and contact.

Table B.1. BD-STEPS Potential Sample of Respondents.

		Annual Number of Interviews by Type of Respondent and Site Type					
Center	Type of Respondent (Mother of…)	Core Computer Assisted Telephone Interview	Linkage to Reportable Infectious Disease	Residual Newborn Bloodspot	Online Occupational Questionnaire	Supplemental Computer Assisted Telephone Interview	Authorization Form for Stillbirth COVID-19 Sub-Study*
	(Form)	**C1**	**D2-D3**	**E2-E5**	**F1**	**G1**	**G6**
Arkansas	Case	270	270	270	87		
	Control	100	100	100	32	100	
	Stillbirth	220				220	10
	Stillbirth						18
California	Case	270	270		87		
	Control	100	100		32		
Georgia	Case	270	270		87		
	Control	100	100		32		
Iowa	Case	270	270	270	87		
	Control	100	100	100	32		
Massachusetts	Case	270	270	270	86		
	Control	100	100	100	32	100	
	Stillbirth	220				220	42
	Stillbirth						87
New York	Case	270	270	270	86		
	Control	100	100	100	32		
North Carolina	Case	270	270	270	86		
	Control	100	100	100	32		
	TOTAL	Total unique respondents = **3,030**	**2,590**	**1,850**	**830**	**640**	**157** (52 previous+105 additional unique respondents)

* Both BD-STEPS participants and non-participants (as demonstrated by the lack of data in the Core Assisted Telephone Interview, etc. columns) will be approached about this consent.

B.2. Procedures for the Collection of Information

State-specific birth defects surveillance data are used to identify case subjects for BD-STEPS. The selection of BD-STEPS controls is described in Section B.1. Once potentially eligible subjects are identified for the study, a clinical geneticist reviews the information abstracted from the medical record to determine if they meet the case definition and are eligible for the study. The first contact, sent by mail to the mothers, is an introductory letter, along with a "Human

Subjects" fact sheet, a "Question and Answer" sheet, Privacy Act Statement, and an "Address Correction Form" sent by the Center from which the case or control subject originated (see **Attachments C2-C6**).

Approximately 10 days after the introductory packet has been sent, the centralized interview contractor makes phone contact with the mother. During this phone call, the interviewer obtains oral consent for the interview and either conducts the interview then or schedules the interview at a time convenient for the mother. The questionnaire is administered using a computer assisted telephone interview (CATI) (see **Attachment C1** for a hard copy of the questionnaire). The script used in the telephone interview (including oral consent) is in **Attachment C7**. The script varies slightly depending on the status of the child: control, living case, deceased case, or stillborn/termination case. 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.

A thank you letter is sent after the telephone interview is completed (**Attachment C8**). A fact sheet describing a request for Release of Reportable Infectious Disease information and a written consent form (**Attachment D1-D2**), are included with the interview thank you letter. Verbal consent scrips are also available (**Attachment D3**). After participants provide consent, they will receive a thank you letter (**Attachment D4**).

For the states that allow CBDRP access to newborn bloodspots and require parental consent, a fact sheet describing the previous collection of newborn bloodspots and why researchers are requesting permission to access any leftover bloodspots is included with the interview thank you letter (**Attachment E1**), as well as a written consent form requesting parental permission to access their infant's bloodspots (**Attachment E2**). For parents of multiples (e.g., twins or triplets), consent for sharing data (including newborn bloodspots) of the siblings that were part of the multiple birth is requested (**Attachment E3**). Verbal consent scrips are also available (**Attachment E4-E5**). After participants consent to access their infant's bloodspots, they will receive a thank you letter (**Attachment E6**).

In addition, participants are asked during the interview if they work in one of eight occupational categories of interest. If yes, participants are sent an introductory invitation via email that includes information about the online questionnaire and a link to the online questionnaire, which varies slightly depending upon the participant's reported occupation (**Attachment F1**). After participants complete the online questionnaire, they will receive a thank you letter (**Attachment F2**).

Finally, two Centers ask women whose pregnancies ended in stillbirth with or without birth defects and mothers of liveborn controls to participate in a supplemental telephone interview that ascertains additional information related to risk factors for stillbirth (**Attachment G1**). Eligible women are sent an invitation that includes information about the interview (**Attachment G2**). At the end of the first interview, the interviewer either obtains oral consent for the supplemental second part of the interview and conducts the interview at that time or schedules the supplemental interview at another time convenient for the mother. The supplemental questionnaire is administered using a CATI (**Attachment G1**). The script used in the telephone interview (including oral consent) is in **Attachment G3**. The script varies slightly depending on the status of the child: control or stillborn case. Participants receive a thank you letter after they complete the second/supplemental telephone interview (**Attachment G4**). A subset of women from these two Centers will also be invited to participate in a COVID-19-related sub-study. Women who experienced a stillbirth between January 1, 2017 and October 31, 2019 who have records of placental and/or fetal tissue samples, regardless of prior participation in the BD-STEPS interview, will be sent a letter and request for written authorization (**Attachments G5-G6)** to have these samples shipped to CDC for COVID-19-related testing.

A large portion of the BD-STEPS interview has been maintained from the previous iteration of the CBDRP's case control study of birth defects risk factors, the National Birth Defects Prevention Study (NBDPS), to make pooling of the CBDRP's NBDPS and BD-STEPS data possible; pooled data will facilitate the analysis of rare exposures and the examination of trends over time. The BD-STEPS interview retained topics including pregnancy history, family history,

multiple births, fertility, maternal conditions and illnesses (including diabetes, genitourinary infections, and fevers), medication and herbal use, emotional stress, physical activity, obesity, alcohol and tobacco use, residential history, occupational history, and demographic characteristics (including race, ethnicity, acculturation status, and education).

B.3. Methods to Maximize Response Rates and Deal with Nonresponse

The response rate during the first year of the NBDPS (1998) was approximately 60% for cases and controls. With the addition of a $20 money order in the introductory packet, interview participation rates increased to over 70% in 2000. Interview participation rates ranged from approximately 60-70% from 2005-2009. As of 2019, BD-STEPS participants are offered an additional token of appreciation upon completing the telephone interview, a $30 gift card is included with the thank you letter mailing, to account for inflation and the well-documented decrease in participation across many studies that employ phone-based interviewing. The token of appreciation amount for the online questionnaire, the newborn bloodspot consent request, and the consent to release reportable infectious disease results is ten dollars for each component. The two Centers contributing to the stillbirth component of the study will send an additional $20 gift card with the thank you letter to women asked to participate in the two-part telephone interview.

B.4. Tests of Procedures or Methods to be Undertaken

Many data elements ascertained in the BD-STEPS interviews are consistent with those from the NBDPS interviews, which makes pooling of the CBDRP's NBDPS and BD-STEPS data possible. BD-STEPS is being conducted at seven locations around the country and data will be used in statistical analyses by collaborators at each of the CBDRP. Data will be released at regular intervals based on completed cohorts defined by expected date of delivery for each calendar year. Several data cleaning steps will be implemented before release of the data.

Innovative questions were previously added for BD-STEPS and approved by OMB, and are

detailed in section A.3. The online occupational questionnaire represents a newer method for data collection for the study that began in 2017. In addition, after the telephone interview, requests to obtain consent for newborn screening bloodspots and release of reportable infectious disease information are sent to participants. Reportable infectious disease information includes data reported to the state health department by medical professionals.

B.5. Individuals Consulted on Statistical Aspects and Individuals Collecting and/or Analyzing Data

The statistical aspects of the design of the BD-STEPS data collection are the responsibility of the Scientific Lead:

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Additional consultation on the development of the BD-STEPS was obtained from the Principal Investigators of the CBDRP. Abt Associates is currently contracted by CDC to manage all BD-STEPS interviewing activities; the Abt Associates primary contact is the following:

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Analysis of BD-STEPS data is the primary responsibility of Dr. Ailes, with assistance from the Principal Investigators of the CBDRP.