

**ZEN Colombia Study**  
**Zika in Pregnant Women and Children in Colombia**

**Supporting Statement: Part A**

**OMB # 0920-1190**

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**Suzanne Gilboa, PhD**  
**Telephone: 404-498-4425**  
**Blackberry : 404-421-4199**  
**Fax: 404-498-3550**  
**E-mail: [suz0@cdc.gov](mailto:suz0@cdc.gov)**  
**Pregnancy and Birth Defects Task Force**  
**CDC Zika Virus Response Team**  
**Centers for Disease Control and Prevention**  
**Atlanta, Georgia 30341**

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**Goal of the study:** The goal of the ZEN Colombia study is to better understand modifiable factors affecting the acquisition of Zika infection among pregnant women and their children in Colombia, and the link between Zika infection during pregnancy and adverse outcomes.

**Intended use:** The data from the ZEN Colombia study will provide critical information leading to evidence-based strategies to prevent ZIKV infection in pregnancy; improved counseling of patients about risks to themselves, their pregnancies, and their children; and effective preparedness for agencies providing services to affected children and families.

**Methods to collect:** The proposed information collection is for a prospective cohort study following pregnant women enrolled in the first trimester, their male partners, and their children at several sites in Colombia. This study will use interview- administered questionnaires at study enrollment and follow-up visits for all participants. Select children will be examined for developmental and other assessments. Study staff will abstract medical records from mothers' prenatal care visits, sick visits, and delivery to capture relevant medical information, male partners' sick visits, and from childrens' medical records to obtain information on diagnoses, test or developmental screening results, medical procedures, and hospitalizations until the child's 4<sup>th</sup> birthday.

**Subpopulation to be studied:** For this Information Collection Request, we will follow a subset of children from 6 months to 2 years of age. We will examine these children at 6, 9, 12, 18, 24 months of age. Prior to the expiration of this Information Collection Request, we will request to examine these infants until 48 months of age.

**How data will be analyzed:** A variety of methods will be used to analyze the data from the ZEN Colombia study. These methods include: descriptive analysis, log-binomial regression, Kaplan-Meier survival analysis and multivariable Cox regression, Wilcoxon rank sum tests, and methods that model complex and longitudinal data. These methods will be used to address the specific research questions described in Section.A2 (below).

## Overview

There is a causal link between Zika virus (ZIKV) infection in pregnancy and microcephaly and other severe fetal brain defects. The Centers for Disease Control and Prevention (CDC) surveillance and research efforts are underway in the United States (U.S.) (including territories, particularly Puerto Rico), Brazil, and Colombia to understand the range of other adverse pregnancy and childhood outcomes associated with Zika infection during pregnancy. However, key knowledge gaps exist that cannot be addressed using surveillance data or retrospective data, and thus there is an urgent need to prospectively study pregnant women in areas of high Zika virus transmission in order to contribute to understanding of:

- Risk factors for ZIKV infection in pregnant women and their infants, including behaviors such as use of mosquito-bite prevention measures or condoms to prevent sexual transmission, and factors associated with maternal-to-child transmission;
- Absolute and relative risk for adverse maternal, fetal, infant, and childhood outcomes associated with ZIKV infection; and
- Modifiers of the risk for adverse outcomes among pregnant women and their children following ZIKV infection, including gestational age at infection, presence of ZIKV symptoms, extended viremia, mode of transmission, prior infections or immunizations, and co-infections.
- Modifiers associated with childhood development in infants exposed to ZIKV in-utero or immediately after delivery.

In early February 2016, the Presidents of the U.S. and Colombia met and agreed that the countries would conduct joint epidemiologic investigations through Colombia's Instituto Nacional de Salud (INS) and the U.S. CDC. These joint research efforts include estimating the prevalence of microcephaly in Colombia, assessing risk factors associated with Zika virus infections and microcephaly, and to better understand the (at that time) potential link between Zika infection and adverse birth outcomes. Please see: <https://www.whitehouse.gov/the-press-office/2016/02/04/fact-sheet-peace-colombia-new-era-partnership-between-united-states-and> for additional details. Following this meeting, CDC received a formal letter of invitation from the Vice Minister of Health of Colombia requesting technical assistance and collaboration regarding the Zika virus epidemic (available upon request). INS and CDC developed multiple projects, including enhanced surveillance of pregnant women with symptomatic Zika virus disease. We now seek to implement a prospective cohort study in which we will follow women enrolled in the first trimester of pregnancy, their male partners, and their children in several cities in Colombia in which ZIKV transmission is currently ongoing.

## A. Justification

### A.1. Circumstances Making the Collection of Information Necessary

The program submits this Information Collection Request as a "Revised" Information Collection Request. The length of data collection request for Office of Management and Budget (OMB) approval is three years. The National Center on Birth Defects and Developmental Disabilities (NCBDDD) at the CDC is making this request as authorized by Section 301 of the Public Health

Service Act (42 U.S.C. 241) (**Attachment A**). The previous standard Information Collection Request (approved on July 26, 2017) was to follow infants up to 6 months of age. However, there are more subtle but detrimental effects on children's long-term development. In order to understand further these long-term effects on all of the primary domains of children's development, we are submitting this revised Information Collection Request to follow these children until 2 years of age. In future Information Collection Requests, we will seek to follow these children until 4 years of age.

ZIKV is a mosquito-borne flavivirus transmitted by *Aedes* species mosquitoes; reports of sexual transmission, mother-to-child transmission, and laboratory-acquired infections also exist. There is also evidence of human ZIKV infection sporadically in Africa and Asia prior to 2007, when an outbreak of ZIKV caused an estimated 5,000 infections in the State of Yap, Federated States of Micronesia. Since then, there is evidence of ZIKV in 65 countries and territories, mostly in Central and South America. Common symptoms of ZIKV in humans include rash, fever, arthralgia, and nonpurulent conjunctivitis. The illness is usually mild and self-limited, with symptoms lasting for several days to a week; however, based on previous outbreaks, some infections are asymptomatic. The prevalence of asymptomatic infection in the current Central and South American epidemic is unknown.

Although the clinical presentation of ZIKV infection is typically mild, ZIKV infection in pregnancy can cause microcephaly and related brain abnormalities when fetuses are exposed *in utero*. Other adverse pregnancy outcomes related to ZIKV infection remain under study, and include pregnancy loss, other major birth defects, arthrogryposis, eye abnormalities, and neurologic abnormalities.

Colombia's INS began surveillance for ZIKV in 2015, reporting the first autochthonous transmission in October 2015 in the north of the country. As of October 2016, Colombia has reported over 105,000 suspected ZIKV cases, over 19,000 of them among pregnant women. The ZEN (Zika en Embarazadas y Niños en Colombia) Colombia study, this translates to Zika in Pregnant Women and Children in Colombia, is a prospective cohort study following pregnant women, their male partners, and their children in Colombia. Given that the Zika virus may transition from outbreak levels to endemic level, it is critical to begin enrollment rapidly to ensure that a large number of pregnant women with Zika virus infection in the first trimester can be enrolled and followed up to assess outcomes. This study supports CDC's mission as authorized in section 301 of the Public Health Service Act (42 U.S.C. 241) (Att A).

In addition to understanding adverse pregnancy and birth outcomes related to ZIKV infection, there is limited research in understanding the long-term effects of ZIKV infection during pregnancy on developing children. Studies anticipate that children with microcephaly will suffer developmental and intellectual delays. Further, studies anticipate that children born to Zika-affected mothers who are phenotypically normal may have impaired developmental trajectories across multiple developmental domains that require further understanding. Therefore, long-term follow-up of children born to Zika-affected mothers is crucial in understanding the range of adverse physical and developmental outcomes associated with ZIKV exposure during pregnancy.

Since receiving emergency OMB approval, the program received approval for the study protocol by the appropriate Colombian scientific and ethics committees. Training of study staff began on January 30, 2017, and the study sites enrolled the first pregnant women on February 9, 2017, in the first city of Barranquilla. Bucaramanga started training on March 28, 2017, and began enrolling on May 15, 2017. Tuluá began training on May 8, 2017, and began enrolling June 25, 2017. We received approval for the standard Information Collection Request on July 23, 2017. As of October 23, 2017, the study sites enrolled 678 pregnant women, 135 male partners, and 70 infants in the study. Enrollment is ongoing. At the time of this revised data collection, we anticipate enrolling and additional 500 pregnant women and 125 male partners.

During the Emergency Clearance period, the project team was able to field quickly the interview-administered questionnaires related to pregnancy at study enrollment and follow-up visits for all participants. Since initial implementation, the program made protocol changes to reflect site-specific needs. These include changes to questionnaires, flyers, and other documents previously approved in the emergency OMB application. The program made these changes to improve comprehension by study participants, reduce participant burden, and capture additional information later found to be necessary for conducting the study. In the standard Information Collection Request, the program added questionnaires for the mothers to assess infant health and development during the 0-6 month follow-up. For this revised information request for child follow-up from 6 months to up to 2 years of age, the program plans to administer questionnaires and other tools related to the child's development, including in physical/motor, language, cognitive, and psychosocial domains. We will also administer questionnaires related to the family environment (including maternal mental health) as well as infant feeding and crying questions.

As cases of new Zika infection during pregnancy is declining over time in Colombia, the first wave of infants born in ZEN will likely be our exposed children who we need to be enrolled and followed for the 6 months to 4 year follow-up to evaluate their development. Our first ZEN infant who was born in June 2017 will be 6 months old in December 2017. Thus, it is critically important that this Information Collection Request is in place so as not to miss the follow-up of eligible children.

## **A.2. Purpose and Use of Information Collection**

CDC's goal in developing the ZEN Colombia study is to understand better the adverse pregnancy, maternal, and child health outcomes associated with ZIKV during pregnancy and early childhood (up to 4 years of age). In addition, the ZEN Colombia study will assess the modifiable factors affecting the acquisition of Zika infection during pregnancy in Colombia. The data from the ZEN Colombia study will provide critical information supporting the evidence-based strategies to prevent ZIKV infection in pregnancy; improved counseling of pregnant women and their partners about risks to themselves, their pregnancies, and their children; and effective preparedness for agencies providing services to affected children and families.



The primary research questions we aim to address with the ZEN Colombia study are:

1. Evaluate associations between ZIKV in pregnancy and adverse pregnancy or maternal outcomes, such as preterm birth, preeclampsia, maternal death, postpartum hemorrhage, and intrapartum fetal demise, among others. We will also explore effect modification by gestational age of infection.
2. Quantify the magnitude of the association between ZIKV infection in pregnancy and major birth defects, with specific focus on microcephaly and congenital Zika syndrome. The prospective design of the study will allow estimation of both absolute and relative risk for microcephaly for women with ZIKV infection during pregnancy.
3. Identify risk factors for symptomatic ZIKV infection in pregnancy among all women with laboratory-confirmed ZIKV in pregnancy. We will consider a spectrum of risk factors, including maternal demographics, ZIKV infection characteristics, and other potential risk factors such as smoking and medication use.
4. Assess modifiers of the risk for adverse outcomes among pregnant women and their young infants following ZIKV infection. These include prenatal factors, such as gestational age at infection, presence of ZIKV symptoms, extended viremia, mode of transmission, prior infections or immunizations, and presence of co-infection with other viruses.
5. Assess modifiers of the risk for adverse outcomes among children ages 6 months – 4 years following ZIKV infection. These include prenatal factors noted above, as well as post-natal factors (e.g., sociodemographic characteristics, family environment characteristics, nutritional status, and environmental hazards).
6. Identify risk factors for symptomatic ZIKV infection in infancy through childhood among infants with laboratory-confirmed ZIKV born to women enrolled in the study. We will consider a spectrum of risk factors, including maternal ZIKV infection in pregnancy factors, co-infections, sociodemographic characteristics, and birth factors.
7. Investigate associations between ZIKV infection in utero or, infancy and children's hearing loss, vision impairment, and other physical and developmental outcomes up through age 4 years.
8. Examine developmental trajectories for children with congenital or infant ZIKV infection from birth to four years of age relative to trajectories for unexposed children.
9. Compare infants with laboratory evidence of congenital Zika virus infection to unexposed infants, to understand risk factors and modifiers of the risk for adverse outcomes (e.g. socioeconomic status, parental stress or depression, social support, nutrition, environmental hazards).
10. Estimate survival of children born to ZIKV infected mothers.

Secondary research questions we aim to address with the ZEN Colombia study are:

1. Identify risk factors for ZIKV infection in pregnant women, partners, and children. We will explore a spectrum of risk factors, including mosquito bites and mosquito bite preventive measures, sexual transmission, sociodemographic characteristics, and medical risk factors. The results of this analysis will provide information on the reduction in risk

associated with adherence to recommended preventive measures and risk factors for infection during pregnancy and among other populations.

2. Identify characteristics associated with taking preventive measures (mosquito bite prevention, sexual transmission) against contracting Zika virus among pregnant women and their partners. The results of this analysis will assist in targeting education or intervention to individuals at greatest risk for Zika infection.
3. Describe symptoms associated with ZIKV and estimate the positive predictive value of certain symptoms or constellations of symptoms in pregnant women, men, and children to allow for refinement of clinical diagnosis of ZIKV infection in a setting in which testing and/or results might not be readily available.
4. Assess the duration of viremia following ZIKV infection and investigate risk factors (such as sociodemographics, comorbidities, and co-infections) associated with prolonged viremia among pregnant women, men, and children with laboratory-confirmed ZIKV infection in blood.

This study is a part of an ongoing public health emergency response related to the Zika virus outbreak in Colombia. Results of this study will be used to guide INS's and CDC's recommendations for surrounding prevention of ZIKV infection in pregnancy and childhood both internationally and domestically; to improve counseling of patients about risks to themselves, their pregnancies, their partners, and their children; and for enhancing preparedness of agencies providing services to affected children and families.

During the Emergency Clearance period, data collection started in February 2017, and we made protocol changes to adjust to the local setting. As of October 23, 2017, the study sites enrolled 678 pregnant women, 135 male partners, and 70 infants in the study. Enrollment is ongoing. The expected total enrollment will be 5,000 pregnant women, 1,250 male partner, 4,500 infants, and a subset of 900 infant/children over the 3 years of data collection requested. The approval for the standard Information Collection Request was received on July 12, 2017 which allowed data collection up to 6 months of age of the infants. The current request is to revise the Information Collection Request to follow these children until 2 years of age.

### **Overview of the Data Collection System**

We will recruit pregnant women in the first trimester of pregnancy at participating clinics in Colombia's private and public health care systems and followed through their pregnancy, delivery, and immediate post-partum period. The Pregnant Woman Eligibility Screener Form (Att B.1; C.1), administered to potential participants by trained ZEN research staff, will be used to confirm participant eligibility prior to consent or assent. At the enrollment visit, study staff will interview pregnant women using the Pregnant Woman Enrollment Questionnaire (Att B.2; C.2) and an Adult Symptoms Questionnaire (Att B.5; C.5). All pregnant women will attend monthly study clinic visits through the end of pregnancy and will be interviewed using the Maternal Follow-Up (Att B.3; C.3) and Adult Symptoms Questionnaires (Att B.5; C.5). Pregnant women will have interval visits (about two weeks after clinic visits) where they will be

monitored for incident ZIKV infection by collection of urine and be interviewed using the Adult Symptoms Questionnaire (Att B.5; C.5), until the middle of the third trimester (approximately 32 weeks gestation). If the study confirms that a woman is ZIKV positive, we will interview her using the Adult Symptoms Questionnaire (Att B.5; C.5) every two weeks and Maternal Follow-Up Questionnaire every month (Att B.3; C.3) until she is negative for two consecutive blood samples. If a woman has a spontaneous fetal demise, she will be interviewed using an Adult Symptoms Questionnaire (Att B.5; C.5) if one has not been completed within seven days prior to the event. At delivery or within 10 days postpartum, the mother will be interviewed using the Infant Symptoms (Att B.6; C.6), Adult Symptoms (Att B.5; C.5), and Maternal Follow-Up (Att B.3; C.3) Questionnaires. All Questionnaires will be conducted in-person (or via telephone if the participant prefers).

Infants of mothers participating in the study will be followed until 6 months of age to detect health outcomes that might not have been detectable at birth. Mothers will be interviewed using the Infant Symptoms Questionnaire (Att B.6; C.6) at each visit and the Ages and Stages Questionnaires (Att B10; C10) at the 2 and 6 month visit. If an infant has symptoms of ZIKV, the mother will be interviewed using the Infant Symptoms Questionnaire (Att B.6; C.6).

We will follow a subset of parent-child pairs from 6 months to 2 years of age. We will examine these parent-child pairs at 6, 9, 12, 18, and 24 months of age. The parent-child pair will be screened for eligibility starting at around 4 months of age using the Parent-Child Follow-up Eligibility Screening Form (Att B8; C8). If eligible, the parents will be consented and asked to give permission for both the parent and child to participate in the follow-up (Att D5). Upon signed consent and permission, the parent/guardian will be interviewed using the Parent-Child Enrollment Questionnaire (Att B.9; C.9). The Parent-Child Follow-up questionnaire will be asked at every subsequent visit (Att B10; C10). In addition, the following validated, standardized and copyrighted assessments will be used at specific visits (Att B12):

- Ages and Stages Questionnaires (Att B.11; C.11) at 12 and 24 months.
- Bayley Scales of Infant and Toddler Development (Att B12) at 12, 18, and 24 months
- Strengths and Difficulties Questionnaire (Att B12) at 24 months
- Peabody Developmental Motor Scales (Att B12) at 24 months
- Parenting Stress Index IV (Att B12) at 6, 9, 12, 18, 24 months
- Center for Epidemiologic Studies Depression scale (Att B12) at 6, 9, 12, 18, 24 months
- Test of Nonverbal Intelligence (Att B12) at 9 months

In addition to administered questionnaires, ZEN Colombia study staff will abstract medical records from mothers' prenatal care, sick visits, and delivery to capture relevant medical information. We will abstract maternal medical records up to six months after delivery to collect information on post-partum medical issues. As part of the current information request, staff will also abstract medical records from children enrolled in the study to obtain information on diagnoses, test and developmental screening results, medical procedures, and hospitalizations as well as clinically assess children until 24 months of age for developmental delays including hearing, vision, cognitive, motor, and language.

We will recruit male partners via their pregnant partners around the time of their partners' enrollment into the study. The Male Partner Eligibility Screener Form (Att B.7; C.7), administered in-person (or via telephone if the participant prefers) to potential participants by trained ZEN research staff, will be used to confirm participant eligibility prior to consent. At enrollment, men will provide a blood sample and will be interviewed using the Male Enrollment Questionnaire (Att B.4; C.4) and Adult Symptoms Questionnaire (Att B.5; C.5). Men will provide urine samples monthly through the second trimester of their partner's pregnancy (about 27 weeks of gestation) to monitor for incident ZIKV infection and be interviewed using the Adult Symptoms Questionnaire (Att B.5; C.5) at the time of each specimen collection. If the male partner is confirmed to have ZIKV, semen will be collected every 2 weeks until semen is negative for ZIKV for two consecutive semen samples or until the partner's pregnancy ends and men will be interviewed using the Adult Symptom Questionnaire (Att B.5; C.5). Study staff will also abstract medical records for male partner's sick visits.

### **Description of Information to be Collected**

Study staff will interview all study participants in either a face-to-face or phone format.

#### **1. *Pregnant Woman Enrollment Questionnaire – Att B.2; C.2***

The study will administer this questionnaire to pregnant women at the time of enrollment, after given consent or assent. The purpose of this questionnaire is to gather demographic, environmental, and behavioral information; health insurance information; medical and pregnancy history; and current knowledge and perceptions about ZIKV.

#### **2. *Maternal Follow-Up Questionnaire – Att B.3; C.3***

The study will administer this questionnaire to participating pregnant women at each monthly prenatal clinic visit and once during the postpartum period (within 10 days of delivery). The purpose of this questionnaire is to gather information about changes in health insurance, risk or protective factors for ZIKV infection, or adverse pregnancy and infant outcomes that may change over the course of a woman's pregnancy.

#### **3. *Male Enrollment Questionnaire – Att B.4; C.4***

The study will administer this questionnaire to male partners of enrolled women at the time of enrollment, after given consent. The purpose of this questionnaire is to gather demographic, environmental, and behavioral information; health insurance information, medical history; and current knowledge and perceptions about ZIKV.

#### **4. *Adult Symptoms Questionnaire – Att B.5; C.5***

The study will administer this questionnaire is administered to pregnant women and their male partners at each clinic visit, interval visit, or any time he or she becomes ill with Zika-like symptoms in between regularly-scheduled visits. The study also asks this questionnaire of the mother in the postpartum period (up to 10 days after delivery). The purpose of this questionnaire is to identify participants who have symptoms compatible with ZIKV, to refer symptomatic participants for ZIKV testing at a participating clinic, to identify healthcare-seeking behavior, and participation in other ZIKV studies.

**5. *Infant Symptoms Questionnaire – Att B.6; C.6***

The study will administer this questionnaire to one of the parents to complete at the postpartum visit, interval visit, or any time the infant becomes ill with Zika-like symptoms in between regularly scheduled visits. The purpose of this questionnaire is to obtain information on possible ZIKV symptoms among participating infants, breastfeeding practices and feeding difficulties among mothers of these infants, changes in health insurance, and participation in other ZIKV studies.

**6. *Parent-Child Enrollment Questionnaire --Att B.9; C.9***

The study will administer this questionnaire to parent/guardian whose child will be participating in the long-term follow-up after enrollment and consent. The purpose of this questionnaire is to gather baseline demographic, environmental, and behavioral information; and health insurance, medical history, financial stress, quality of relationship information.

**7. *Parent-Child Follow-up Questionnaire --Att B10; C10***

The study will administer this questionnaire to parent/guardian whose child will be participating in the long-term follow-up at every visit after the 6 month visit. The purpose of this questionnaire is to gather environmental and behavioral information; and health insurance, medical history, financial stress, quality of relationship information.

**8. *Ages and Stages Questionnaires – Att B.11; C.11***

This screening tool is administered to one of the parents or guardians when the infant is approximately 2, 6, 12, and 24 months of age. All infants will receive the 2 month questionnaire when the child is 2 months old. At 6, 12, and 24 months, infants will receive the questionnaire that corresponds to their chronological age or adjusted age, if the infant was born preterm. The purpose of this questionnaire is to identify potential developmental delays in the child.

**9. *Bayley Scales of Infant and Toddler Development -- Att B.12***

This tool includes involvement of the parent and children through direct, manipulation-based assessment of children's skills/abilities (physical, cognitive, language domains) and parent-report measures of early childhood development (psychosocial, adaptive behavior) across broad domains. Parents and child will complete the Bayley at 12, 18, and 24 months of child age. The purpose of this tool is to gain in-depth information about children's development, compare children's development across domains and chart child's developmental change across all domains over time.

**10. *Strengths and Difficulties Questionnaire – Att B.12***

This tool is a parent-reported "symptom" measure of children's emotional and behavior problems, with good ability to discriminate between psychiatric and non-psychiatric populations. Parents will report on children's emotional problems, conduct problems, hyperactivity, peer problems, and prosocial behaviors at 24 months. This tool can be

used to compare children’s emotional and behavioral problem behaviors across multiple domains of psychosocial adjustment and chart children’s problem behavior over time. Provides cutoff scores to indicate clinically relevant problem behavior.

**11. *Peabody Developmental Motor Scales – Att B.12***

This tool involves in-depth direct, manipulation/play-based assessment of children’s motor skills. The Peabody captures more subtypes of children’s motor development than the Bayley, and would provide a more “full phenotype” developmental assessment in the area of early childhood physical and motor development. This tool will be administered at 24 months, an optimum time for assessment of motor development. The purpose of this tool is to pinpoint the exact nature of children’s physical/motor deficits, compare children’s development on the full domain of physical/motor skills, and provide “age equivalent” scores and percentile ranks.

**12. *Parenting Stress Index IV – Att B.12***

This tool is a parental self-report of stress related to parenting across three domains: parental distress (characteristics of parent), parent-child dysfunctional interaction (characteristics of the parent-child relationship), and difficult child (characteristics of child). This tool will be administered at 6, 9, 12, 18, and 24 months. It can be used to identify families with high levels of parenting stress, compare family environment quality across children, and provides both raw scores and “clinical cutoffs” for what constitutes clinically stressful parenting that can be used for **only** research purposes (not for referral).

**13. *Center for Epidemiologic Studies Depression Scale – Att B.12***

This tool is a parental self-report of adult depressive symptoms in the past week. This tool will be administered at 6, 9, 12, 18, and 24 months. It can be used to compare raw parental depressive scores across parents in study and proportions of parents that meet the “clinical cutoff” (considered depressed).

**14. *Test of Nonverbal Intelligence – Att B.12***

This tool is a direct, manipulation-based assessment of adult intelligence, aptitude, abstract reasoning, and problem solving. This tool will be administered at one time point to the parent, ideally around the child’s 9 month birthday. This assessment is language free, and is ideal for those with limited language ability and diverse backgrounds.

**How Information Will Be Shared and for What Purpose**

There are three main entities involved in the conduct of the ZEN Colombia study. Colombia’s INS is CDC’s scientific collaborator on this study. CDC employs a contractor, Vysnova Partners, Inc., to conduct the ZEN Colombia study in collaboration with INS. All CDC and contractor personnel who have access to protected data are required to go through training on confidentiality protections and to sign a nondisclosure agreement (Att F.1, F.2, F.3).

Patients’ personally identifiable information (PII) will not be disclosed in any reports, statistical summaries, or shared or disclosed to public entities, external agencies, or other people or

organizations outside the entities involved in the conduct of the ZEN Colombia study. We have engaged in discussions with researchers at the National Institute of Health who are launching the ZIP pregnancy cohort in several countries, including Colombia and the Center for Global Health at CDC who will be providing technical assistance to several smaller pregnancy cohorts in Guatemala, Kenya, Thailand and Haiti. Globally, there is growing interest in harmonization across these studies, to be ultimately able to conduct traditional aggregate data meta-analyses or individual participant data meta-analyses based on pooled de-identified data. If there is any possibility of sharing of de-identified data with selected researchers such as those noted here, we will certainly engage INS in any decision to do so. Currently, our plan is to share statistical summaries of de-identified data in peer-reviewed journals and conference presentations.

### **A.3. Uses of Improved Information Technology and Burden Reduction**

The ZEN Colombia study questionnaires have been designed to collect the minimum amount of information necessary to meet the study's objectives. Questions about other factors with the potential to have mediating or moderating effects on primary outcomes have been considered and included. All questionnaire data will be obtained by trained interviewers via questionnaires administered to participants. All data will be entered and stored on the password-protected and secure web-based data collection system, which will be housed on an INS server in Colombia.

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

While many experts agree that ZIKV causes microcephaly, more studies are needed to better understand the full spectrum of defects and other adverse pregnancy and childhood outcomes caused by congenital ZIKV infection, to quantify the relative and absolute risks of these outcomes among children who are born to women who were infected at different times during pregnancy, and to identify factors that modify the risk of an adverse pregnancy, birth, or childhood outcomes (see Rasmussen et al., *N Engl J Med* 2016; 374:1981-1987). There is an urgent need to prospectively study pregnant women in areas of high Zika virus transmission because many of these key knowledge gaps cannot be addressed using surveillance data or retrospective data. Because of its prospective design, the ZEN Colombia study can systematically identify the timing of symptomatic and asymptomatic infections in pregnant women, the latter of which cannot be ascertained from surveillance data or retrospective studies. The prospective design also allows estimation of absolute risk of adverse outcomes, including less severe outcomes that may not yet have been identified, in addition to relative risk, because the study has a well-defined base population. The ZEN Colombia study is the only data source that collects comprehensive information of ZIKV infection initiating in the first trimester and associated birth defects and physical/developmental outcomes from multiple sites in Colombia.

As part of its Zika response efforts, CDC is collaborating with the INS in Colombia, which has had the second-most cases of the mosquito-borne Zika virus after Brazil. The large number of cases and stage of the outbreak in Colombia provides an opportunity to collect actionable information on a shorter timeframe than is possible elsewhere. We expect this collaboration to provide critical scientific information to help the United States, Colombia, and other countries

prepare for the unprecedented challenges posed by Zika. We timed participant enrollment to coincide with the expected second wave of Zika virus cases in Colombia, the peak time for infection, and will provide CDC with the ability to rapidly obtain answers to questions about Zika that will help to shape the course of this public health emergency response.

The U.S. National Institutes of Health (NIH) partnered with Fiocruz Institute in Brazil to launch a five-country prospective cohort study (the Zika in Infants and Pregnancy, or “ZIP” study) to evaluate the risk of ZIKV infection among pregnant women and their infants. ZIP is enrolling in different countries to compare and contrast the clinical manifestations and risk factors in different countries, and looking at environmental as well as co-infections that could affect outcome. In addition, enrolling in different countries maximizes the chance of capturing Zika infections in the cohort since the epidemic trajectory is hard to predict. Since the beginning of the Zika outbreak, CDC and the U.S. NIH have been in close communication. More recently, CDC and NIH have been collaborating to harmonize data collection efforts between the ZEN Colombia Study and the NIH ZIP study as some of the research questions are aligned. This harmonization will be critical for making meaningful comparisons between geographic regions, and strengthens the contributions of both studies to the pressing public health research questions. In addition, we could pool the common data points across multiple pregnancy and infant cohort studies to have sufficient power to examine the full spectrum of adverse clinical outcomes of Zika virus infection during pregnancy including less common outcomes. To this end, CDC, U.S. NIH and other governmental and non-governmental organizations are participating in an international effort led by World Health Organization to pool individual participant level data to both compare and contrast risk of Zika infection on adverse outcomes.

There are some differences to note. NIH does not collect specimens from associated male partners in all sites. The ZEN Colombia study aims to assess the relative contribution of sexual transmission and mosquito-borne transmission to occurrence of infections in pregnancy. In addition, Zika outbreak dynamics may vary according to location. While the NIH study is an international collaboration, ZEN is an intensive, prospective data collection effort focused specifically on Colombia in 3 cities (Barranquilla, Bucaramanga, and Tulua). The Colombian site for the NIH study is located in Cali. The same pregnant women will not participate in both studies, as the ZEN study eligibility requirement includes being enrolled for prenatal care at the study sites, and no study sites are enrolling for both studies. ZEN will address questions to inform Emergency Response Efforts specified by the Colombian government, which the US government has committed to helping INS address, as specified in the agreement between the US and Colombian Presidents, as described above.

In general, the ZEN Colombia study is the only prospective cohort study of pregnant women currently being undertaken by CDC. Although surveillance efforts focused on ZIKV in pregnancy are currently underway in the U.S. (including territories) and Colombia, the ZEN study is the only CDC-based project that will allow

- Study of both symptomatic and asymptomatic pregnant women with ZIKV infection; and
- Estimation of the absolute risk of microcephaly and other adverse outcomes among pregnant women infected with Zika virus during different gestational ages, which is not



possible using a case-control design

**Ongoing projects in the CDC Zika response and how the ZEN Colombia study fills gaps not addressed by these existing efforts**

<b>Project</b>	<b>Contribution added by ZEN</b>
<b>Persistence of Zika virus in semen and urine of adult men in the United States with confirmed Zika virus infection (OMB Control No. 0920-1139)</b>	Study population includes only adult men with Zika virus infection; one objective of ZEN includes examining persistent viremia specifically in pregnant women
<b>Zika virus persistence in body fluids of patients with Zika virus infection in Puerto Rico (ZIPER Study) (0920-1140)</b>	Study population includes all ages and sexes; one objective of ZEN includes examining persistent viremia specifically in pregnant women
<b>The Effect of Community-Wide Vector Control Initiatives on Zika Virus Transmission in Puerto Rico, 2016 (0920-1137)</b>	Not applicable – ZEN does not address community-wide vector control
<b>Evaluation of In2Care Traps during the Zika Outbreak in Puerto Rico (0920-1071)</b>	Not applicable – ZEN does not address community-wide vector control
<b>Knowledge, Attitudes, and Practices related to a Domestic Readiness Initiative on Zika Virus Disease (0920-1136)</b>	Not applicable – ZEN does not address a specific domestic readiness objective
<b>Integrated Aedes aegypti Vector Control Intervention in Caguas City, Puerto Rico to Prevent and Control Zika Virus Infections (PRA N/A)</b>	Not applicable – ZEN does not address community-wide vector control
<b>Migrant Farm Workers Understanding and Use of Measures to Prevent Zika Transmission (0920-1126)</b>	Not applicable – ZEN does not address migrant farm workers
<b>US Zika Pregnancy Registry (0920-1101 0920-1143)</b>	This project focuses on U.S. pregnant women with laboratory evidence of Zika virus infection; Voluntary reporting to the registry may result in ascertainment bias, while ZEN will prospectively identify pregnant women in early pregnancy. In addition, the ZEN study includes collection of data from maternal questionnaires.
<b>Assessment of Interventions Intended to Protect Pregnant Women in Puerto Rico from Zika virus infections (0920-1118)</b>	Not applicable – ZEN does not assess the effectiveness of specific interventions in preventing Zika virus infection
<b>Assessment of Contraceptive Use and Needs, Puerto Rico, 2016 (0920-1114)</b>	Not applicable – ZEN does not assess contraceptive use and needs

<p><b>Enhanced Surveillance of Pregnancy and Infant Outcomes following with Zika Virus infection in Pregnancy, Colombia (PRA N/A)</b></p>	<p>ZEN will prospectively identify pregnant women in early pregnancy and collect data from maternal questionnaires, rather than relying solely on medical records, as is done in this surveillance effort; the surveillance data do not allow identification of absolute risk, because the base population is challenging to quantify. Further, because infections are identified retrospectively, exact timing of infection during pregnancy cannot be ascertained. Only symptomatic pregnant women are included in the surveillance project, while ZEN will allow identification of both symptomatic and asymptomatic pregnant women.</p>
<p><b>Characterization of Guillain-Barré Syndrome Cases in the Setting of Zika Virus Transmission— Colombia, 2016 (PRA N/A)</b></p>	<p>ZEN does not focus on Guillain-Barré Syndrome as an outcome</p>
<p><b>Formative Evaluation of Zika Prevention Kits for Pregnant Women in Puerto Rico (0920-1071)</b></p>	<p>ZEN does not propose evaluation of Zika Prevention Kits</p>
<p><b>Case-control microcephaly study in Brazil (0920-1011)</b></p>	<p>ZEN will start with a defined base population of pregnant women at risk for Zika infection in their first trimester of pregnancy and prospectively identify timing of infection in this cohort of pregnant women, which will allow estimation of the absolute risk of microcephaly and other adverse outcomes. Retrospective case identification is vulnerable to selection bias, particularly in relation to symptomatic infection. Further, a case-control study can only estimate relative risk.</p>
<p><b>Collection of serum and plasma from patients with antibodies reactive with Zika virus and other arboviruses (PRA N/A)</b></p>	<p>ZEN focuses specifically on pregnant women and their infants</p>
<p><b>Mosquito Surveillance Survey (0920-1101)</b></p>	<p>Not applicable – ZEN does not propose to assess mosquito populations</p>
<p><b>American Samoa Zika Surveillance (0920-1011)</b></p>	<p>ZEN will prospectively identify pregnant women in early pregnancy and collect data from maternal questionnaires, rather than relying solely on medical records, as is done in this surveillance effort; the surveillance data do not allow identification of absolute</p>

	risk, because the base population is challenging to quantify. Further, because infections are identified retrospectively, exact timing of infection during pregnancy cannot be ascertained. ZEN will allow identification of both symptomatic and asymptomatic pregnant women.
<b>Case-control GBS study in PR – Surveillance (0920-1106)</b>	ZEN does not focus on Guillain-Barré Syndrome as an outcome
<b>Case-control GBS study in PR - Records Abstraction (PRA N/A)</b>	ZEN does not focus on Guillain-Barré Syndrome as an outcome
<b>Formative evaluation among partners of pregnant women about Zika in PR (0920-0572)</b>	Not applicable – ZEN does not include formative evaluation of any programs
<b>Zika Postpartum Emergency Response Survey, Puerto Rico (0920-1127)</b>	ZEN will ask mothers immediately postpartum information on Zika symptoms to go along with the specimen collected as well as a follow-up questionnaire to assess changes in risk and behavior since the last study visit. These questions build on each other, rather than being a point-in-time survey.
<b>Monitoring &amp; Evaluation for the Zika Contraception Access Network (0920-1164)</b>	Not applicable – ZEN does not monitor and evaluate contraceptive use and needs
<b>Zika Virus RNA Persistence in Pregnant Women and Congenitally Exposed Infants in Puerto Rico (PRN to be assigned)</b>	ZEN will prospectively identify pregnant women in early pregnancy in addition to assessing prolonged viremia in pregnant women.

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

We will collect data from private and public health care systems in the study cities in Colombia, including some that may be small businesses. The study data collection elements are the absolute minimum required for the intended use of the data. We will present the survey instruments in a clear and easy to complete format based on previous surveys and recommendations from survey methodology research.

#### **A.6. Consequences of Collecting the Information Less Frequently**

Each woman will participate starting in the first trimester of her pregnancy through the first 6 months of her baby’s life. Each male partner will participate, until about 27 weeks of gestation of his partner’s pregnancy or if ZIKV positive, until the end of his partner’s pregnancy. A subset of mothers, fathers, or another legal guardian (one per family) will participate until children reach 4

years of age. Infants will participate for the first 6 months of life and a subset until 4 years of age. It is important to monitor health status for mothers throughout pregnancy and their babies' childhood, particularly for mothers with ZIKV infection or caring for children who might be affected by ZIKV in multiple visits. It also important to monitor the health status of infants and children affected by ZIKV across multiple visits as growth and development changes throughout early childhood. Male partners will be monitored for ZIKV infection. The data collection frequency is essential to answer questions about transmission of ZIKV, adverse maternal, fetal, and childhood outcomes following ZIKV infection in pregnancy, and risk factors for infection and adverse outcomes. Collecting information less frequently may not permit this determination.

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

This information collection fully complies with all guidelines of 5 CFR 1320.5.

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

A 60-Day Federal Register Notice was published in the Federal Register on August 30, 2017. Vol. 82, NO. 167, pp. 41265. No public comments were received.

CDC has consulted with other public health agencies, e.g., NIH, to ensure there are no duplication of similar efforts in the study location.

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

Participants may be provided a transportation cost that covers expenses incurred for travel and for meals that will be set in accordance with the local economy and recent research studies conducted with this population. The intent of the per diem is to minimize personal financial outlay of participants for their time and travel. This plan will be reviewed by a governmental ethics committee in each participating city in Colombia in accordance with Colombian research guidelines.

The actual amounts may be adjusted for each city based on what is appropriate for the local economy. These may be given to the participant in the form of cash, transportation tickets, or as determined by the cities as appropriate and within Colombian research guidelines. The cost value will range from 0 to 20,000 Colombian pesos (~0-7 USD) for any single trip and 0 to 12,000 pesos (~0-3 USD) for meals. If the local recommendation in a given study site is to not provide any cost coverage, then in that site, nothing will be provided.

#### **A.10. Protection of Privacy and Confidentiality of Information Provided by Respondents**

Data will be collected as information in identifiable form (IIF) therefore the Privacy Act does apply. Records are covered under CDC Privacy Act System of Records Notice (SORN) No. 0920-0136 “Epidemiologic Studies and Surveillance of Disease Problems” and SORN No. 09-20-0113, “Epidemic Investigation Case Records Systems Notice.” The compilation of individual research results and responses into a study database for the ZEN Colombia study will be used only for research purposes. Investigators have completed certifications in Information Security and Privacy Awareness and will put systems in place to meet Privacy Act requirements. The sections below describe the protections in place to preserve privacy and confidentiality.

ZEN study site staff will protect the confidentiality of participant data and research records by assigning a unique study Participant Identification Number (PIN) to all study forms, specimens, and database. To ensure the anonymity of the research data, this PIN will be the only identifier associated with a subject’s research data, such as their questionnaire responses, developmental assessments, physical exams, laboratory results, and abstracted medical information. An electronic crosswalk file that is separate from the research data will be kept to provide the link between the unique subject PIN and associated PII (e.g. names, dates of birth, contact information, etc.). Resulting reports or publications regarding this research are to be reported in aggregate and ensure individuals cannot be identified. A number of procedures and security measures are in place to protect patient privacy. At clinical sites, study forms will be stored in a locked file cabinet that only study staff can access. Study data will be stored on a password-protected database that only study staff can access. Patients’ personally identifiable information (PII) will not be shared or disclosed to public entities, external agencies, or other people or organizations outside the entities conducting the ZEN Colombia study. CDC’s Institutional Review Board oversees certain types of data analysis conducted with this information collection, and the confidentiality of information submitted by patients and clinics is protected by an Assurance of Confidentiality under Section 308(d) of the Public Health Service Act. CDC has an Assurance of Confidentiality for this study (Appendix F.1). INS employees are not covered by this Assurance of Confidentiality.

During the administration of the informed consent or assent document, ZEN study staff will explain to respondents that participation is voluntary, they can end their participation at any time without negative consequences. An informed consent and assent for the collection of data has been approved (Att D.1, D.2, D.3, D.4, and D.5).

The informed consent and assent documents (Att D.1, D.2, D.3, D.4 and D.5) clearly explain that the study findings will be compiled and only presented on a group level, with no individuals identified. Participants are also told that relevant test results will be shared with their doctors and insurance companies. In addition, within the informed consent or assent document, there is a separate item where the participant must check “Yes” or “No” regarding their approval to allow researchers store study samples and health information for future research.

Paper documentation, such as the questionnaires and documentation of informed consent or assent, will be stored in a designated and secured office area and similarly designated and locked filing cabinet within each study site. Research data will be stored in on online database and will

be kept secure and confidential on the INS server, requiring user authentication and password protection. Administrator controls in place include regular backups, security training, completion of a security certification and accreditation (C&A), security plans, and policies. Access to ZEN Colombia study data is limited to CDC, INS, and contractor staff supporting the project. The contractor follows federal security requirements and adheres to all CDC security policies and regulations. Requirements for adherence to privacy provisions and policies, as well as instructions for destruction of study data and files when the contract ends, are specified in the contract language.

#### **A.11. Institutional Review Board (IRB) and Justification for Sensitive Questions**

The CDC Institutional Review Board (IRB) approved the study as Research (Att E.1). The protocol was reviewed in accordance with the expedited review process outlined in 45 CFR 46.110(b)(1), Categories 2, 5, and 7. The IRB determined the study to be not greater than minimal risk to subjects. The IRB approved the inclusion of children under 45 CFR 46.404 and the inclusion of pregnant women under 45 CFR 46.204. A first CDC IRB amendment was approved on January 3, 2017, a second amendment on January 30, 2017 a third amendment on March 06, 2017, a fourth amendment on July 11, 2017, a fifth amendment on August 14, 2017, a sixth amendment on September 05, 2017 and seventh amendment on 10/23/2017. INS approval was received on 12/12/16 (Att E.2). Vysnova reliance to CDC IRB was received 9/26/16 (Att E.3).

The participating IRBs will also conduct continuing reviews of routine annual data points as well as required review of any adverse events or protocol violations as needed. Some data to be collected for ZEN Colombia may be sensitive in nature to some respondents. To reduce the sensitivity of these questions, respondents will be completing questionnaires in private and will be reminded that they are not required to answer any questions to which they would prefer not to respond. Topics that may be perceived by subjects as sensitive are: 1) patient demographic information including social-economic status; 2) patient medical history including number of pregnancies lost; 3) Zika knowledge, symptom and diagnosis information; 4) sexual behavior and practice, and alcohol or drug use; 5) pregnancy outcome information; 6) child health information, 7) parent mental health and other family environment information.

CDC developed the data collection requirements after extensive consultation with medical professionals and epidemiologists. There is consensus that the sensitive information collected is necessary to provide accurate information of the ZIKV infection in order to identify associated risk factors and adverse maternal, fetal, and child adverse outcomes following ZIKV infection in pregnancy.

#### **A.12. Estimates of Annualized Burden Hours and Costs**

## Burden Hours

Respondents are pregnant women (and subsequently, mothers) and their male partners who agree to participate in the study.

ZEN Colombia study staff will use the Eligibility Screener Questionnaire to confirm eligibility of pregnant women. Because it is administered prior to initiation of the consent process, the burden estimate for administration of the ZEN Screener Questionnaire is based on a larger pool of pregnant women than that of women eligible and consented for the ZEN study. This assumes 25% of women screened will not meet eligibility criteria. The remainder of the burden estimate is based on completion of questionnaires by consented respondents: 5,000 pregnant women, 1,250 male partners, 4,500 newborns, and a subset of 900 infants. This assumes a 25% participation rate among male partners and that 90% of infants are live born.

As exhibited in Table A.12-1, each study questionnaire instrument is considered one response. The annualized burden hours for each questionnaire was calculated by multiplying the number of respondents by the number of responses (estimated number of times each questionnaire would be completed) per respondent by the average burden per response.

The total estimated annualized burden for all information collection for ZEN is 14,210 hours. The Number of Respondents requested for the Information Request was based on the Number of Respondents that the Program estimated annually.

### A. 12 – 1 Estimated Annualized Burden Hours

Respondents	Form Name	No. of Respondents	No. of Responses (Questionnaires) per Respondent	Average Burden per Response (in hours)	Total Burden Hours
Pregnant women	Pregnant women eligibility questionnaire	600	1	5/60	50
	Pregnant women enrollment questionnaire	500	1	35/60	292
	Adult symptoms questionnaire	500	15	10/60	1,250
	Pregnant women follow-up	500	8	15/60	1,000

questionnaire				
Infant symptoms questionnaire	2,250	14	10/60	5,250
Parent-Child Eligibility Questionnaire	1000	1	5/60	83
Parent-Child Enrollment Questionnaire	900	1	20/60	300
Parent-Child Follow-up Questionnaire	900	4	15/60	900
Ages and Stages Questionnaire: 2 and 24 Month Visits	2,250	2	15/60	1,125
Ages and Stages Questionnaire: 12 and 24 Month Visits	900	2	15/60	450
Bayley Scales of Infant and Toddler Development	900	3	30/60	1,350
Strengths and Difficulties Questionnaire	900	1	5/60	75
Peabody Developmental Motor Scales	900	1	30/60	450
Parenting Stress Index IV	900	5	10/60	750
Center for Epidemiologic Studies Depression Scale	900	5	5/60	375
Test of Nonverbal Intelligence	900	1	20/60	300



Male partners	Male partner eligibility questionnaire	150	1	5/60	12
	Male enrollment questionnaire	125	1	25/60	52
	Adult symptoms questionnaire	125	7	10/60	146
Total					14,210

**a) Estimated Annualized Cost to the Federal Government**

Information for the ZEN Colombia study may be collected by nurses, social workers, data entry clerk, field study staff, lab technicians, physicians, or developmental specialists.

**A. 12 – 2 Annualized Cost to Respondents**

Type of Respondents	Form Name	Number of Respondents	Number of Responses per Respondent	Average Burden Hours per Response	Total Burden Hours	Hourly Wage Rate	Total Costs
Pregnant women	Pregnant women eligibility questionnaire	600	1	5/60	50	\$2.50 USD*	\$125
	Pregnant women enrollment questionnaire	500	1	35/60	292	\$2.50 USD*	\$ 730
	Adult symptoms questionnaire	500	15	10/60	1,250	\$2.50 USD*	\$ 3,125
	Pregnant women follow-up questionnaire	500	8	15/60	1,000	\$2.50 USD*	\$2,500
	Infant symptoms questionnaire	2,250	14	10/60	5,250	\$2.50 USD*	\$ 13,125

	Parent-Child Eligibility Questionnaire	1000	1	5/60	83	\$2.50 USD*	\$207.50
	Parent-Child Enrollment Questionnaire	900	1	20/60	300	\$2.50 USD*	\$750
	Parent-Child Follow-up Questionnaire	900	4	15/60	900	\$2.50 USD*	\$2,250
	Ages and Stages questionnaire: 2 and 6 month visits	2,250	2	15/60	1125	\$2.50 USD*	\$2,812.50
	Ages and Stages Questionnaires: 12 and 24 Month Visits	900	2	15/60	450	\$2.50 USD*	\$1,125
	Bayley Scales of Infant and Toddler Development	900	3	30/60	1,350	\$2.50 USD*	\$3,375
	Strengths and Difficulties Questionnaire	900	1	5/60	75	\$2.50 USD*	\$187.50
	Peabody Developmental Motor Scales	900	1	30/60	450	\$2.50 USD*	\$1,125
	Parenting Stress Index IV	900	5	10/60	750	\$2.50 USD*	\$1,875
	Center for Epidemiologic Studies Depression Scale	900	5	5/60	375	\$2.50 USD*	\$937.50
	Test of Nonverbal Intelligence	900	1	20/60	300	\$2.50 USD*	\$750
Male partners	Male partner eligibility questionnaire	150	1	5/60	12	\$2.50 USD*	\$30

	Male enrollment questionnaire	125	1	25/60	52	\$2.50 USD*	\$ 130
	Adult symptoms questionnaire	125	7	10/60	146	\$2.50 USD*	\$ 365
<b>Total</b>							<b>\$ 35,525</b>

\*Source: UN International Labour Organization estimate of average monthly wage in Colombia (in 2015) divided by 160 hours/month ([http://www.ilo.org/ilostat/faces/home/statisticaldata/ContryProfileId?\\_adf.ctrl-state=ydigxis12\\_154&\\_afLoop=691022007511742#!%40%40%3F\\_afLoop%3D691022007511742%26\\_adf.ctrl-state%3Dxcdb4823a\\_4](http://www.ilo.org/ilostat/faces/home/statisticaldata/ContryProfileId?_adf.ctrl-state=ydigxis12_154&_afLoop=691022007511742#!%40%40%3F_afLoop%3D691022007511742%26_adf.ctrl-state%3Dxcdb4823a_4))

### A.13. Estimates of Other Total Annual Cost Burden to Respondents or Record Keepers

There are no additional costs to respondents other than their time

### A.14. Annualized Cost to the Federal Government

Estimates of annualized costs to the federal government are included in the following table. Revision of the data collection period will modify annualized costs which include a new contract that will follow a subgroup of children up to 2 years of age.

<b>A. 17 – 1 Annualized Cost to the Federal Government</b>	
ZEN Colombia Study	
<b>Contract</b>	<b>Annualized Cost</b>
1. Total labor	\$126,035.17
2. Total other direct costs	\$2,280,122.04
3. Total overhead	\$150,193.67
4. General and administrative expense	\$203,178.67
5. Fee @ 8%	\$78,486.43
<b>Subtotal</b>	<b>\$2,838,015.97</b>
<b>CDC FTEs</b>	<b>Salary</b>
1. Epidemiologist, GS-601-14/15	\$228,500

2. Epidemiologist, GS-601-13	\$160,000
3. Health Scientist, GS-601-13	\$117,660
4. Statistician, GS-1529-13	\$67,500
5. Public Health Analyst, GS-1529-13	\$67,500
<b>Subtotal</b>	\$641,160
<b>Total Federal Government Cost</b>	<b>\$3,479,175.97</b>

The annualized cost to the federal government is \$3,479,175.97. During the three year data collection period of this this ICR there will be two contracts in place, one contract will cover 18 months of the project and one that covers 15 months with Vysnova as well as CDC staff time to oversee and collaborate on the study. The annual cost of the contract with Vysnova is \$2,838,015.97, which includes operational costs, contractor personnel, facilities, equipment, supplies, laboratory diagnostic tests, developmental and family assessment tools, and materials necessary to assist CDC with the ZEN Colombia study. CDC staff members provide technical oversight and expertise, including analytic and scientific guidance, on ZEN and to the contract staff. CDC staff members participate in reviewing study protocol, implementation, and attend site visits. CDC staff also conducts scheduled calls to monitor the contractor’s performance and ensure that the contractor is meeting project standards and that the data are of high quality, thus ensuring accurate reporting and generation of valid success rates. CDC staff listed in table A.14-1 dedicates approximately 100% of their time to these activities.

**A.15. Explanation for Program Changes or Adjustments**

This is a revised collection of information. In order to understand further the long-term effects on all of the primary domains of children’s development, we are submitting this Revision request to follow 900 children until 2 years of age. Based on the previous burden hours of 20,848 hours, the current total burden hours (14,210 hours) reflects 1) decrease in burden hours because of lowering number of remaining respondents to 500 pregnant women and 125 male partners during the pregnancy follow-up, as enrollment is progressing, and 2) increase in burden hours with the addition of data collection to follow 900 children from 6 months to 2 years of age.

**A.16. Plans for Tabulation and Publication and Project Time Schedule**

The program is requesting a 3-year OMB clearance to cover all data collection activities, including enrollment, follow-up and data analysis. Table A.16 below outlines the project time

schedule after OMB approval. Analysis plans included conducting descriptive and modeling analyses. We will disseminate results of the study to the scientific community through the published literature and presentation at meetings. In concert with dissemination to the scientific community, we will create a rollout plan in collaboration with INS's and CDC's communications teams to release lay versions of the study results to the public, as warranted. Routes of communication include press releases, media interviews, INS or CDC websites, and social media.

**Project Time Schedule**

	Study Year 1				Study Year 2				Study Year 3-4			
	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec	Jan - Mar	Apr - Jun	Jul - Sep	Oct - Dec
Pregnancy enrollment												
Pregnancy study visits												
Male enrollment												
Male study visits												
6-month infant follow up												
6-month to 4-year follow-up												
Data analysis, publications												

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

We request no exceptions from display of expiration date.

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

We seek no exemptions to certification.