**PHASE III RCT OF THE EFFECTIVENESS OF SILVER DIAMINE FLUORIDE IN ARRESTING CAVITATED CARIES LESIONS**
**UNIVERSITY OF MICHIGAN**

**CONSENT TO BE PART OF A RESEARCH STUDY**

| | |
|---|---|
| **TITLE:** | Phase III RCT of the Effectiveness of Silver Diamine Fluoride in Arresting Cavitated Caries Lesions |
| **PROTOCOL NO.:** | 17-094-E<br>WIRB® Protocol #20181760<br>HUM00147622 |
| **SPONSOR:** | National Institute of Dental and Craniofacial Research (NIDCR) |
| **CO-INVESTIGATORS:** | Margherita Fontana, DDS, PhD<br>1011 N. University Room 2393<br>Ann Arbor, Michigan 48109-1078<br>United States<br><br>Carlos Gonzalez-Cabezas, DDS, MSD, PhD<br>1011 N. University Ave<br>CRSE Room 2395<br>Ann Arbor, Michigan 48109-1078<br>United States |
| **STUDY-RELATED PHONE NUMBER(S):** | Carlos Gonzalez-Cabezas, DDS, MSD, PhD<br>734-615-8270<br>734-936-6266, extension 30685 (24 hours) |

## INFORMATION ABOUT THIS FORM

Your child could be eligible to take part in a research study. This form gives you and your child important information about the study. It describes the purpose of the study, and the risks and possible benefits of participating in the study.

Please take time to review this information carefully. After you have finished, you should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or other doctors) about your participation in this study. If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

## 1. GENERAL INFORMATION ABOUT THIS STUDY AND THE RESEARCHERS

**1.1 Study title:** Phase III Randomized Clinical Trial of the Effectiveness of Silver Diamine Fluoride in Arresting Cavitated Caries Lesions

**1.2 Company or agency sponsoring the study:** National Institute for of Dental and Craniofacial Research

**1.3 Names, degrees, and affiliations of the researchers conducting the study:**

Margherita Fontana, DDS, PhD, Department of Cariology, Restorative Sciences, and Endodontics, University of Michigan School of Dentistry
Carlos Gonzalez-Cabezas, DDS, PhD, Department of Cariology, Restorative Sciences, and Endodontics, University of Michigan School of Dentistry

## 2. PURPOSE OF THIS STUDY

**2.1 Study purpose:** The traditional treatments for cavities involve drilling teeth and placing fillings or removing the teeth. Drilling requires teeth to be numbed with an injection. When a young child has many and/or advanced cavities, the child often needs to be treated after being put to sleep. Because being put to sleep has risks for children, there is a need to find other ways to treat cavities in children. This study compares silver diamine fluoride (SDF), a medical substance, to placebo for treating cavities in baby teeth. Children in the study will receive either SDF or placebo painted on cavities in their baby teeth. A placebo is an inactive substance that looks like the study drug, but contains no medication. SDF is currently being used in other countries to treat cavities. The Food and Drug Administration (FDA) has approved SDF for treating sensitivity in teeth, but not for treating cavities in children. Use of SDF in this study is considered investigational. Comparing SDF to placebo will let us know what SDF really does to cavities in baby teeth, and will help us see if SDF stops cavities from progressing.

## 3. INFORMATION ABOUT STUDY PARTICIPANTS (SUBJECTS)

Taking part in this study is completely **voluntary**. You and your child do not have to participate if you don't want to. You may also leave the study at any time. If you do not participate, or if you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

**3.1 Who can take part in this study?** We are looking for children ages 1 to 5 years (12 to 71 months, up until the day they turn 6 years old), who have advanced cavities in at least one of their baby teeth.

**3.2 How many people (subjects) are expected to take part in this study?**
We expect 1,144 children and their parent/legal guardian to take part in the study across three sites: the University of Michigan, New York University, and the University of Iowa.

## 4. INFORMATION ABOUT STUDY PARTICIPATION

**4.1 What will happen to my child and me in this study?**
We will identify cavities in your child's baby teeth that can be treated. Children in this study will be assigned to one of two groups. We'll use a random method (like flipping a coin) to decide which group your child will be in. Your child will have an equal chance of being in each group.

- Children in the first group will have SDF painted on the cavities. The SDF will be painted on twice: at the first visit and again at the 6-month visit.
- Children in the second group will have placebo painted on the cavities. The placebo will be painted on twice: at the first visit and again at the 6-month visit.

Neither the SDF nor placebo will require drilling or numbing medicine. The cavity in the baby tooth could turn dark brown or black in either the SDF or placebo group.

Children in both groups should continue to receive all preventive treatments normally provided to children with cavities. This could be through your Head Start/early childhood education center or dental provider (for example, fluoride varnish, fluoride toothpaste and toothbrush for home use, and instructions on what causes cavities and how to prevent them). Children should not receive any fluoride varnish on the day of SDF or placebo treatment and should not use fluoride toothpaste the evening of the treatment.

We will see you and your child again for check-up visits about three months, six months, and eight months after the first treatment. If your child was enrolled at school, you may not need to be present for the check-ups and we will call you to ask the study questions asked at these visits. We will call you about one and a half, four and a half, and seven months after the first visit to ask you some questions. We will ask you if your child has pain from cavities or if your child has had any problems after the treatment with SDF or placebo. We will ask about any dental care your child has received from dentists outside the study.

We will also call you to ask some questions about 24-48 hours after we treat the cavities at the first visit and 6-month visit. Your child will also be seen for a check-up about 24-48 hours after the first visit and 24-48 hours after the 6-month visit.

We may also call you to schedule and remind you of appointments.

At each visit, we will check your child's teeth, and possibly take photos of your child's teeth. Although the photos could appear in presentations or publications, people will not be able to identify your child. We will ask you to complete surveys about your child's mouth and teeth. At each visit we will let you know of all cavities we find.

Any of your child's teeth that are treated in the study are considered "study teeth." If a cavity in a study tooth starts to cause pain, that tooth will be removed from the study. We will give you a referral to a dentist for treatment for that tooth outside of the study with traditional treatment options, such as fillings with numbing medicine or pulling the tooth. If your child has other study teeth, we will continue to check those teeth during the rest of the study. At the end of the study, we will help you to get a follow-up dental visit set up for your child for traditional treatment that is needed at that time. Section 8 of the consent reviews payment for dental treatment.

**4.2 How much of my time will be needed to take part in this study?**
This study will require six dental visits for your child (the first visit, check-ups at 3 months, 6 months, and 8 months, and check-ups about 24-48 hours after the treatments at the first visit and the 6-month visit). The first visit will take approximately 45 minutes, with most of the time involving paperwork you will complete and about 10 minutes involving the exam for your child. Each check-up dental visit after the first visit will take approximately 10 minutes for an exam for your child, and 10 minutes for you to answer some questions. You may be able to complete the paperwork before the first visit and/or answer the questions for the check-ups over the phone or online. The check-up visits 24-48 hours after the first visit and 24-48 hours after the 6-month visit will take approximately 5 minutes. You will also be required to complete other phone surveys lasting five to ten minutes over the course of the eight months to make sure your child is doing well.

Visits may be arranged at your child's Head Start Center or School, at one of your local providers such as dental/medical clinics, or another secure location. You do not need to be present at visits if they happen during the Head Start or School day.

**4.3 When will my participation in the study be over?**
Participation is expected to end eight months after the first visit.

It is possible that we'll want to stay in contact with you and your child for longer than 8 months. We may also ask you to take part in other studies. At the end of this form, you can tell us if we may contact you about additional visits or studies. Even if you give us permission to contact you later, you don't have to come for future visits or take part in other studies if you don't want to.

## 5. INFORMATION ABOUT RISKS AND BENEFITS

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed on this form about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors.

**5.1 What risks will my child and I face by taking part in the study? What will the researchers do to protect us against these risks?**
Examples of some risks related to the study include:

- The tooth cavity could turn a dark color (although many cavities are already dark in color), and you or your child may not like how it looks.
- The SDF or placebo might not prevent the cavity from getting bigger. A tooth with a cavity could cause pain for your child or could become infected during the study. If this happens, your child might need to see a dentist outside the study to receive treatment.
- Your child may experience a metallic or bitter taste when the solution is put on.
- Temporary discoloration of the gums near the treated cavity after SDF application21,.
- ,Temporary irritation of soft tissues (e.g., redness or ulceration of the skin or mucous membranes) after SDF or placebo application.
- 
- Possible allergic reaction or stomach problems.
- Sensitivity when drying the tooth for the dental exam (this risk is no greater than the risk from a traditional dental examination).
- Cross-contamination (germ-spreading; this risk is no greater than the risk from a traditional dental examination).
- You may not feel comfortable answering questions we ask.
- It is possible that people outside the study might find out your child participated (loss of confidentiality).
- Your child could cry during the exam.

The researchers will try to minimize these risks by first ensuring that the tooth is healthy enough to qualify for the study treatment. We will closely monitor your child and his/her teeth after application of SDF/placebo, at all other study visits, and by phone. If your child's tooth becomes painful or infected, we will give you a referral to a dentist so your child can receive care for the tooth. Your child's teeth will be dried prior to SDF/placebo application, gauze will be used to protect soft tissues and excess fluid will be blotted dry after application to reduce risk of gum irritation. The examiners are dentists who are trained to work with children. Our trained study staff will use the best infection control procedures to stop germs from spreading. Study records are locked in cabinets or maintained on an encrypted database, and a study number is assigned to you and your child. You should contact the study team (see Section 10, below), if you have any concerns.

As with any research study, there could be additional risks that are unknown or unexpected.

**5.2 What happens if my child gets hurt, becomes sick, or has other problems as a result of this research?**
The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured as a result of your being in the study, call the study doctor at the telephone number listed in the contact section of this form. The study doctor will either treat you or send you to another doctor for treatment. You will get free medical

care for any complication, injury, or illness caused by the study drug, device, or procedure. The study sponsor and the study doctor are responsible for determining whether your condition was the result of your participation in the study. The study sponsor will pay for your treatment only if the need for treatment has been caused by the study drug, device or procedure. This means that you or your health plan must pay for any treatment that is part of your usual medical care or that is related to a medical condition you had before participating in the study.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

The researchers have taken steps to minimize the risks in this study. Even so, your child may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that your child has during this study. You should also tell your regular doctors or dentists.

If you believe your child has been injured as a result of this study contact the study doctor, who will help arrange treatment. You or your insurance company will be billed for this care.

**5.3 If my child and I take part in this study, can we also participate in other studies?**
Being in more than one research study at the same time, or even at different times, could increase the risks to you. It could also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

**5.4 How could my child and I benefit if we take part in this study? How could others benefit?**
Potential benefits to you and your child include:

- SDF may stop the cavity from progressing, decrease pain and improve quality of life.
- Because your child's teeth will be examined several times during the study, you may learn early about problems with your child's teeth. Children with serious dental problems will be offered an appointment for an unscheduled study visit and referred for dental care.

The anticipated long-term benefit is that the participation of you and your child in our study could be of great value to the dental community and parents of young children like you if we find SDF is a good treatment for cavities in baby teeth. Right now, the traditional treatment your child would get at the dentist (not SDF) involves fillings or pulling the teeth, requiring teeth to be numbed with an injection. In many cases with young children who have many and/or advanced cavities, the child needs to be treated after being put to sleep. This has the potential to harm the child's brain, or development, and can even cause death in rare cases. If SDF is proven effective, you will be helping in providing evidence about a cost-effective and non-invasive option as an alternative for traditional treatment for cavities in young children.

**5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?**
Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

## 6. OTHER OPTIONS

**6.1 If I decide not to take part in this study, what other options do I have?**
If you choose not to enroll in the study, you could decide to seek treatment for your child elsewhere. If you decide not to participate in the study, we recommend your child be treated for his/her cavities in a dental clinic of your choice.

## 7. ENDING THE STUDY

**7.1 If I want to stop participating in the study, what should I do?**
You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you otherwise would be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving could be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information" (below).

**7.2 Could there be any harm to me or my child if I decide to leave the study before it is finished?**
If you decide to leave the study prior to its completion, it is extremely important to notify the Study Coordinator listed in Section 10. Some of your child's teeth could need additional treatment if they are not being checked regularly, and these teeth should be treated soon after exiting the study. It is important that your child receive dental treatment if not being closely checked by the investigators of this study. If you wish to exit the study, the study team can help you find a dentist.

**7.3 Could the researchers take my child and me out of the study even if I want to continue to participate?**
Yes. There are many reasons why the researchers might need to end your participation in the study. Some examples are:

- ✓ The researcher believes that it is not in your child's best interest to stay in the study.
- ✓ You and/or your child become ineligible to participate.
- ✓ Your child's condition changes and he/she needs treatment that is not provided as part of the study.
- ✓ You do not follow instructions from the researchers.
- ✓ The study is suspended or cancelled

## 8. FINANCIAL INFORMATION

**8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?**
There are no costs for participating in this study. At the end of the study, or if a study tooth is removed from the study because it is decided it needs a different treatment, and you go and get the treatment, you and/or your health plan will be billed for all the things you would have been responsible to pay for if you were not in the study, like:

- X-rays,
- Fillings, and
- Extractions.

The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured as a result of your being in the study, call Dr. Gonzalez immediately, at 734-763-3391. The doctor will either treat you or send you to another doctor for treatment.

You will get free medical care at the University of Michigan Health System (UMHS) in Ann Arbor, MI for any hospitalization or ER visits directly caused by the study drug, device, or procedure. The UMHS and the study doctor are responsible for determining whether your condition was the result of your participation in the study.

The UMHS will pay for your treatment only if the need for treatment has been caused by the study drug, device or procedure. This means that you or your health plan must pay for any treatment that is part of your usual medical care or that is related to a medical condition you had before participating in the study.

It is not the policy of the federal funding agencies to compensate or provide medical treatment for human subjects in federally funded studies.

By signing this form, you do not give up your right to seek payment if you are harmed as a result of being in this study.

**8.2 Will I be paid or given anything for taking part in this study?**
Yes. For completing both the dental exam and parent questionnaires, the parent/legal guardian will receive $125 ($100 for completing the in person visit and $25 for completing the study questionnaires) for each of the four main study visits (first visit, and 3, 6 and 8 month visits or withdrawal visit). Also, the parent/legal guardian will be paid $25 for completing each of the three phone surveys (at 1.5, 4.5, and 7 months). For participation in the two in person 24- to 48-hour visits (after the first visit and 6 month visit) participants will receive $25 for each.

If we need to see your child for an unplanned visit, up to $30 may be provided for transportation/parking to attend those visits.

During the study, if a tooth that the study is treating needs additional treatment from a dentist outside the study, and if you provide us proper receipts for the care of that study tooth within 6 months after the study tooth is withdrawn from the study, you can receive up to $250 to cover treatment costs.

No payment will be provided for scheduling/reminder phone calls/contacts. Your child will also be given a small gift (valued less than $3) after each study visit, along with a toothbrush and toothpaste.

In order to pay you for your participation, we need to collect your name, address and social security number or taxpayer identification number.

**8.3 Who could profit or financially benefit from the study results?**
The investigators who conduct this study will not profit or financially benefit from the study results. The companies who manufacture the SDF may benefit financially. Those companies are not directly associated with this study, but the results of this study could help these companies get permission from the FDA to market SDF for treatment of cavities, if it is proven to work in this study.

## 9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how your privacy and the confidentiality of your research records will be protected in this study.

**9.1 How will the researchers protect my child's and my privacy?**
After treatment and each follow-up visit is completed, the information for the teeth treated will be recorded in a secure database that does not contain your or your child's personal information, such as

name, address, and Social Security number. All records are placed in a secure location, and no study photographs will contain identifying information.

**9.2 What information about my child or me could be seen by the researchers or by other people? Why? Who might see it?**
Signing this form gives the researchers your permission to obtain, use, and share information about you and your child for this study, and is required in order for you and your child to take part in the study. Information about your child may be obtained from any hospital, doctor, and other health care provider involved in your child's care, including:

- Health plan/health insurance records; Dental plan/dental insurance records
- Any records relating to your child's condition, the treatment received, and response to the treatment
- Billing information
- Personal identifiers

There are many reasons why information about you and your child may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to check your child's exam results or look for side effects to report if your child has had any problems.
- University, the Institutional Review Board (IRB), Food and Drug Administration (FDA) and/or other government officials may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly,
    - Learn more about side effects, and
    - Analyze the results of the study.
- Insurance companies or other organizations may need the information in order to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your School of Dentistry electronic health record.
- If you receive any payments for taking part in this study, the accounting department from the University of Michigan may need your name, address, social security number or taxpayer identification number, payment amount, and related information for tax reporting purposes.
- Federal or State law may require the study team to give health information to agencies, for example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are or that you participated.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

University of Michigan policies require that private information about you be protected. This is especially true for your personal health information.

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described earlier it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) and may be redisclosed without your permission.

**9.3 What happens to information about me after the study is over or if I cancel my permission?**
As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your and your child's information.
- To provide limited information for research, education, or other activities (This information would not include your or your child's name, social security number, or anything else that could let others know who you or your child are).
- To help University and government officials make sure that the study was conducted properly.

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

Your permission will not expire unless you cancel it. You may cancel your permission at any time by writing to the researchers listed on the first page of this form.

As long as your information is kept within the University Health System, it is protected by the University's Health System's privacy policies. For more information about these policies, ask for a copy of the University's "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA) and may be further shared without your permission.

**9.4 When does my permission expire?**
Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you cancel your permission no new information will be collected about your child.

## 10. CONTACT INFORMATION

**10.1 Who can I contact about this study?**
Please contact the researchers listed below to:

- Obtain more information about the study.
- Ask a question about the study procedures or treatments.
- Talk about study-related costs to you or your health plan.
- Report problems with study payments.
- Report an illness, injury, or other problem (you may also need to tell your regular doctors).

- Leave the study before it is finished.
- Express a concern or complaint about the study.

**University of Michigan Contact: Carlos Gonzalez, DDS, MSD, PhD**
**Mailing Address: 1011 N University Ave; CRSE Rm 2393; Ann Arbor, MI 48109**
**Telephone: 734-615-8270 or 734-936-6266, extension 30685 (24 hours)**
**Email: michigansdf@umich.edu**

You may also express questions, concerns or complaints about a study, or if you have questions about your rights as a research subject by contacting the Institutional Review Board listed below

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

An IRB is a group of people who perform independent review of research studies.

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (number that begins HUM that is located at the top or bottom of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

## 11. RECORD OF INFORMATION PROVIDED

**11.1 What documents will be given to me?**
Your signature in the next section means that you have received copies of all of the following documents:

- This "Consent to be Part of a Research Study" document. (Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University medical record.)

## 12. SIGNATURES

**Consent/Assent to Participate in the Research Study**
Assent of children is NOT required because the capability of all subjects will be so limited that they cannot reasonably be consulted.

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with _____. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my and my child's participation as research subjects, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request.

Child's Legal Name: _____

Parent/Legal Guardian's Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

**Extra visits (optional):**
We may want to start a new follow-up study in the future. If we do, please let us know if you would allow us to contact you.

Please check one:

☐ Yes, I am willing to be contacted if another study starts
☐ No, I am not willing to be contacted if another study starts

Initials_____ Date_____

**Principal Investigator or Designee**

I have provided this participant with information about this study that I believe to be accurate and complete. The participant indicated that he or she understands the nature of the study, including risks and benefits of participating.

Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____