Human Subjects Protocol (HSP)

Form Version: October 15, 2008

- **You are applying** for IRB review of the research described in this form.
- **To avoid delay**, respond to all items in order and include all required approvals and documents.
- **To complete the form**, click the underlined areas and type or paste in your text; double-click checkboxes to check/uncheck. For more tips, see www.uab.edu/irb/forms.
- **Mail or deliver all materials to AB 470**, 701 20th Street South, Birmingham, AL 35294-0104.

Indicate the type of review you are applying for:

☒ Convened (Full) IRB *or*

☐ Expedited—See the Expedited Category Review Sheet, and indicate the category(ies) here: ☐1 ☐2 ☐3 ☐4 ☐5 ☐6 ☐7

1. IRB Protocol Title: Comparison of Clinpro™ 5000 1.1% Sodium Fluoride Anti-Cavity Toothpaste, Clinpro™ Tooth Crème, and MI-Paste Plus for the Prevention and Reduction of White Spot Lesions in Orthodontic Treatment

2. Investigator, Contacts, Supervisors

a. Name of Principal Investigator: Chung How Kau
Degree(s)/Title: BDS, MScD, MBA, PhD, FDS, FAMS(Ortho), FFD (Ortho)/Professor & Chair
Dept/Div: Orthodontics Mailing Address: SDB 305 UAB ZIP:0007 BlazerID: ckau
Phone: 4-1289 Fax: 5-7590 E-mail:ckau@uab.edu

b. Name of Contact Person: Teri Baginski Title: Research Coordinator
Phone: 4-4547 Fax: 5-7590 E-mail: shadia@uab.edu
Mailing Address (if different from that of PI, above): SDB 307, zip 0007

INVESTIGATOR ASSURANCE STATEMENT & SIGNATURE

By my signature as Principal Investigator, I acknowledge my responsibilities for this Human Subjects Protocol, including:

- Certifying that I and any Co-Investigators or Other Investigators comply with reporting requirements of the UAB Conflict of Interest Review Board;
- Certifying that the information, data, and/or specimens collected for the research will be used, disclosed and maintained in accordance with this protocol and UAB policies;
- Following this protocol without modification unless (a) the IRB has approved changes prior to implementation or (b) it is necessary to eliminate an apparent, immediate hazard to a participant(s);
- Verifying that all key personnel listed in the protocol and persons obtaining informed consent have completed initial IRB training and will complete continuing IRB training each year;
- Verifying that all personnel are licensed/credentialed for the procedures they will be performing, if applicable;
- Certifying that I and all key personnel have read the *UAB Policy/Procedure to Ensure Prompt Reporting of Unanticipated Problems Involving Risks to Subjects or Others to the IRB, Institutional Officials, and Regulatory Agencies* and understand the procedures for reporting;
- Applying for continuing review of the protocol at least annually unless directed by the IRB to apply more frequently;
- Conducting the protocol as represented here and in compliance with IRB determinations and all applicable local, state, and federal law and regulations; providing the IRB with all information necessary to review the protocol; refraining from protocol activities until receipt of initial and continuing formal IRB approval.

Signature of Investigator:_____ **Date:**_____

c. List all staff who will be involved with the design, conduct, and reporting of the research, their degree(s) and job title, and any additional qualifications. Include individuals who will be involved in the consent process. *Repeat the table below for each individual.*
Note. For studies involving investigational drugs, include all investigators who will be listed on FDA Form 1572 and attach a copy, if applicable. Send the IRB a copy of Form 1572 anytime you update the form with the FDA.

Role:	☐Co- -*OR*- ☒Other –*AND/OR*- ☒Consent Process
Full Name:	Teri Baginski
Primary UAB Dept.: (Employer if not UAB)	Orthodontics
Degree(s) / Job Title:	Research Coordinator
Additional Qualifications pertinent to the study:	____

d. Is the principal investigator a student, fellow, or resident? ☐Yes ☒No
If Yes, complete items below and obtain signature of faculty advisor or supervisor:

Supervisor's Name:	____
Degree(s) / Job Title:	____
Additional Qualifications pertinent to the study:	____
Telephone:	____
E-Mail:	____
Signature:	_____

e. Describe the principal investigator's activities related to this protocol and provisions made by the PI to devote sufficient time to conduct the protocol:
Dr. Kau will compare Clinpro™ 5000 1.1% Sodium Fluoride Anti-Cavity Toothpaste, Clinpro™ Tooth Crème, and MI-Paste Plus for the prevention and reduction of white spot lesions during orthodontic treatment.

f. Is medical supervision required for this research? ☐Yes ☒No
If Yes, who will provide the supervision?
☐ PI will provide -*OR*- Name:____ Telephone:____
If other than PI, obtain signature of person providing medical supervision:
Signature: _____

g. Describe the process that ensures that all persons assisting with the research are adequately informed about the protocol and their research-related duties and functions:
IRB Training Certification

3. Funding

Is this study funded? ☒Yes ☐No
If No, specify that costs of the study will be covered by funds from the UAB department or other source named:____
If Yes, attach one copy of completed application or request for funding sent to sponsor, and complete a-d.
a. Title of Grant or Contract: Comparison of Clinpro™ 5000 1.1% Sodium Fluoride Anti-Cavity Toothpaste, Clinpro™ Tooth Crème, and MI-Paste Plus for the Prevention and Reduction of White Spot Lesions in Orthodontic Treatment
b. PI of Grant or Contract: Chung How Kau
c. Office of Grants & Contracts Administration Link or Tracking Number: T_____
(*or enter "Pending" and provide upon receipt from OGCA*)
d. Sponsor, Funding Route (*check and describe all that apply*):
☐ Government Agency or Agencies—Agency name(s):____
☐ NIH Coop. Group Trial—Group name:____

☐ Private Nonprofit (e.g., Foundation)—Name:____
☒ Industry, investigator-initiated—Name: Indiana Nanotech
Describe the funding arrangement: See Exhibit B of Clinical Trial Agreement between the Board of Trustees and Indiana Nanotech (attached)
Note. Western IRB reviews industry-sponsored protocols unless the investigator initiated the research, or the study qualifies for expedited review or involves gene therapy.
☐ UAB Departmental/Division Funds—Specify:____

4. Conflict of Interest—Human subjects research involving a disclosed financial interest is subject to IRB review following review by the Conflict of Interest Review Board.

The following definitions are used for Item #4:

Immediate family means spouse or a dependent of the employee. *Dependent* is any person, regardless of his or her legal residence or domicile, who receives 50% or more of his or her support from the public official or public employee or his or her spouse or who resided with the public official or public employee for more than 180 days during the reporting period.

Financial Interest Related to the Research means financial interest in the sponsor, product or service being tested, or competitor of the sponsor.

For each investigator and staff member involved in the design, conduct and reporting of the research (2a. and c.) answer the questions below: **(Repeat the section below for each individual)**

Name: Chung How Kau

Do you or your immediate family have any of the following? (check all that apply)

☐ An ownership interest, stock options, or other equity interest related to the research of any value.
☐ Compensation related to the research unless it meets two tests:
- Less than $10,000 in the past year when aggregated for the immediate family.
- Amount will not be affected by the outcome of the research.

☐ Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright, or licensing agreement.
☐ Board of executive relationship related to the research, regardless of compensation.

Name: Teri Baginski

Do you or your immediate family have any of the following? (check all that apply)

☐ An ownership interest, stock options, or other equity interest related to the research of any value.
☐ Compensation related to the research unless it meets two tests:
- Less than $10,000 in the past year when aggregated for the immediate family.
- Amount will not be affected by the outcome of the research.

☐ Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright, or licensing agreement.
☐ Board of executive relationship related to the research, regardless of compensation.

If you checked any of the above, a financial interest disclosure has to be submitted to or currently be on file with the CIRB. A completed CIRB Evaluation has to be available before the IRB will conduct its review.

5. Locations Involved

a. Describe the facilities available for the conduct of the research. For research on UAB campus, include building names and room numbers: UAB Orthodontics Clinic, School of Dentistry Building third floor, SDB 305

b. Indicate all "performance sites" that will provide space, services, facilities, potential or actual participants, or other support for this protocol.
☐ The Kirklin Clinic (TKC)

☐ University of Alabama Hospital (UAHosp)
☐ The Children's Hospital of Alabama (TCHA)
☐ Callahan Eye Foundation Hospital (CEFH)
☐ UAB Highlands
☐ Jefferson County Dept. of Health (JCDH)
☐ Birmingham Veterans Affairs Medical Center (BVAMC)
☐ General Clinical Research Center (GCRC)—inpatient
☐ General Clinical Research Center (GCRC)—outpatient
☐ General Clinical Research Center (GCRC) at The Kirklin Clinic (TKC)
☐ Other (i.e., Any performance site not listed above, including those covered by subcontracts related to this protocol)—Describe:____

c. Is this study a clinical trial requiring clinical services at one of the performance sites listed in Item b above? ☐Yes ☒No
If Yes, Fiscal Approval Process (FAP)-designated units complete a FAP submission and send to fap@uab.edu. For more on the UAB FAP, see www.uab.edu/ohr.

d. Is this a field study? ☐Yes ☒No
If Yes, describe the community:

e. Is the study to be undertaken within a school, business, or other institution that does not have an institutional review board? ☐Yes ☒No
If Yes, attach a statement of any contacts with and approvals from the appropriate institution officials.
Note. Documentation of all such approvals must be received by the UAB OIRB before IRB approval will be issued.

f. Has this protocol or project been reviewed by another IRB, similar review board, or departmental review committee(s) that authorizes the use of its patient populations? ☐Yes ☒No
If Yes, provide name of the review board(s):____
and for each board listed, enter either the date of latest approval(s) or "PENDING":____
or reasons not approved:____.
If this protocol is subsequently rejected or disapproved by another review board, the UAB IRB must be notified promptly.
Attach copies of approvals/disapprovals.

g. Will any of the participants be from the Birmingham Veterans Affairs Medical Center? ☐Yes ☒No
If Yes, attach VA IRB approval or notification from the VA Research and Development Department that the study has been submitted to the VA IRB for review.

h. Will the study be conducted at or recruit participants from the Jefferson County Department of Public Health (JCDH)? ☐Yes ☒No
If Yes, attach notification that the protocol has been approved by JCDH or the Alabama Department of Public Health IRB.

6. Multi-Site Studies

a. Is the investigator the lead investigator of a multi-site study? ☐Yes ☒No
b. Is UAB a coordinating site in a multi-site study? ☐Yes ☒No
c. If you answered **Yes** to *a* or *b*, describe the management of information obtained in multi-site research that might be relevant to the protection of participants. Include, at a minimum, the following items:
- IRB approvals from other sites

- Unanticipated problems involving risks to participants or others. (For example, if there is an unanticipated problem involving risks to participants or others, which site is responsible for reporting it?)
- Interim results.
- Protocol modifications.

7. Drugs: Will any drugs or supplements be used/studied in this protocol? ☐Yes ☒No
If Yes, attach the Drug Review Sheet.

8. Devices: Will any devices be studied in this protocol or used for a purpose other than for which they were approved by the FDA? ☐Yes ☒No
If Yes, attach the Device Review Sheet.

9. Special Approvals

a. Does this project involve the use of radioisotopes? ☐Yes ☒No
If Yes, attach documentation of approval from the Radiation Safety Division.

b. Does this project include patients with contagious infections (e.g., mumps, measles, chickenpox, TB, meningitis)? ☐Yes ☒No
If Yes, attach documentation of approval from Chairman of the Infection Control Committee of the appropriate facilities.

c. Does this project involve obtaining remnant biopsy or surgical material from the Department of Pathology or any other source? ☐Yes ☒No
If Yes, attach documentation of approval from the entity or individual providing the materials (e.g., the UAB Division of Anatomic Pathology Release of Pathologic Materials).

d. Does this project require obtaining any remnant clinical laboratory specimens, body fluids, or microbiological isolates from the Department of Pathology or any other source? ☐Yes ☒No
If Yes, attach documentation of approval from the entity or individual providing the materials (e.g., the UAB Division of Laboratory Medicine Release of Pathologic Materials).

e. Does this project use stored (existing) specimens from a repository? ☐Yes ☒No
If Yes, attach documentation of approval for use of specimens, and describe how existing specimens are labeled:____

10. Use of Specimens

Does this project involve collecting specimens from participants and storing them for future research? ☐Yes ☒No
If Yes, complete a-h. If no, skip to Item 11

a. How will specimens be obtained, processed, distributed, and stored?

b. How will specimens be labeled (e.g., unique identifier, medical record number, Social Security number, name, date of birth)?

c. How will clinical data associated with the specimens be collected and stored?

d. What participant-identifying information will be collected and linked to the specimens?

e. What steps will be taken to maximize the confidentiality of linked identifiers? For example, procedures could include using a password-protected computer database to link identifiers, with limited personnel knowledgeable of the password, or coded identifiers released without the ability to link to clinical data (also called "stripped" or "anonymized" specimens).

f. Will specimens be shared with other investigators in the future? ☐Yes ☒No
If Yes, what identifiers, clinical information and demographic information will be shared; or will the specimens be stripped of identifiers (i.e., anonymized)? Also **if yes**, outline your procedure for assuring IRB approval for release and use prior to release of specimens.

Note. Investigators who receive and/or use these specimens must document approval from the appropriate IRB(s) before the specimens may be released.

g. Will biological samples be stored for future use? ☐Yes ☒No
If Yes, indicate whether they will be used for the disease under study in this protocol or research on other diseases.

h. Is genetic testing planned? ☐Yes ☒No
If Yes, describe the planned testing here and see "DNA/Genetic Testing" in the Guidebook for consent requirements.

11. Gene Therapy

Does this project involve gene therapy or administering recombinant materials to humans? ☐Yes ☒No

If Yes, submit the Gene Therapy Project Review Panel Report –OR- If this is a vaccine trial that is exempt from the NIH Guidelines For Research Involving Recombinant DNA Molecules, submit the Protocol Oversight Review Form For Clinical Vaccine Trials.

12. HIPAA Privacy and Security

Will the PI or others obtain, review, or make other use of participants' "personal health information" (i.e., information, whether oral or recorded in any form or medium that (a) is created or received by a health care provider and (b) relates to past, present, or future physical or mental health or condition of an individual; or provision of health care; or payment for provision of heath care)? ☒Yes ☐No

If Yes, complete a-e as described.

a. Will the data/information be stored or managed electronically (on a computer)? ☒Yes ☐No

b. Is the principal investigator requesting that the UAB IRB waive patient HIPAA authorization from another institution or entity (e.g., insurance company, collaborating institution). **If Yes**, attach copy of privacy notices from institution/entity, and provide the name of institution/entity:____ ☐Yes ☒No

c. Indicate which, if any, of the listed entities below would provide information or maintain health information collected for this protocol and/or where health information that been collected will be stored/maintained.

- ☐ The Kirklin Clinic
- ☐ University of Alabama Hospital
- ☐ The Children's Hospital of Alabama
- ☐ Callahan Eye Foundation Hospital
- ☐ UAB Highlands
- ☐ Jefferson County Department of Health
- ☒ School of Dentistry
- ☐ School of Health Professions
- ☐ School of Medicine
- ☐ School of Nursing
- ☐ School of Optometry
- ☐ University of Alabama Health Services Foundation
- ☐ UAB Health Centers
- ☐ Viva Health
- ☐ Ophthalmology Services Foundation
- ☐ Valley Foundation
- ☐ Medical West - UAB Health System Affiliate

Health System Information Systems:

- ☐ HealthQuest
- ☐ Cerner Millennium (Lab, Radiology, UED, Surgery)
- ☐ EMMI - Master Member Index
- ☐ Horizon - IPV (IVR/CDA/CRIS)
- ☐ CareFlow Net
- ☐ Eclipsys (PIN)
- ☐ IMPACT
- ☐ None—**If None, skip to Item 13.**

d. Indicate which of the listed identifiers would be associated/linked with the protected health information (PHI) used for this protocol.

- ☒ Names
- ☐ Geographic subdivisions smaller than a State
- ☐ Elements of dates (except year) related to an individual
- ☒ Telephone numbers
- ☐ Fax numbers
- ☐ Email addresses
- ☐ Social security numbers
- ☐ Medical record numbers
- ☐ Health plan beneficiary numbers
- ☐ Account numbers
- ☐ Certificate/license numbers
- ☐ Vehicle identifiers and serial numbers
- ☐ Device identifiers and serial numbers
- ☒ Biometric identifiers
- ☐ Web universal resource locators (URLs)
- ☐ Internet protocol address numbers
- ☒ Full-face photographic images
- ☐ Any other unique identifying number—Describe:____

Note. Codes are not identifying as long as the researcher cannot link the data to an individual

☐ None—**If None, skip to Item 13.**

e. Choose one plan to describe your use of the personal health information:

☐ The data collected meet the specifications for a "limited data set"
—Attach Data Use Agreement or Business Associate Agreement

☒ Research staff will obtain authorization from each patient to use the information
—Attach Patient Authorization form, complete except for patient name and IRB protocol number

☐ PI requests Waiver of Patient Authorization to use the information
—Attach Waiver of Authorization and Informed Consent form

PROPOSED RESEARCH

- The IRB will not accept grant applications and/or sponsor's protocols in lieu of the items as outlined below.
- Do not separate responses from items. Instead, insert your response to each item below the item, keeping the information in the order of this form.
- Number each page of the Human Subjects Protocol (i.e., Page *X* of *Y*).

13. Purpose—in nontechnical, lay language

Summarize the purpose and objectives of this protocol, including any related projects, in one short paragraph.

The purpose of the study is to determine if Clinpro™ 5000, Clinpro™ Tooth Crème, or MI-Paste Plus has an effect on the formation and resolution of white spot lesions for patients undergoing orthodontic treatment. This study will include 90 patients in the UAB Orthodontic Clinic.

14. Background—in nontechnical, lay language

Summarize in 2-3 paragraphs past experimental and/or clinical findings leading to the formulation of this study. Include any relevant past or current research by the Principal Investigator. For drug and device studies summarize the previous results (i.e., Phase I/II or III studies).

During the course of orthodontic treatment, the practitioner normally faces two common iatrogenic treatment side effects: root resorption and enamel decalcification, with the latter occurring at a much higher frequency. While the processes that lead to enamel demineralization are understood, methods to diminish or perhaps eliminate degradation of enamel surfaces are being searched for. Several approaches have been formulated to counteract demineralization of tooth structure. One approach involves patient compliance and consists of in-depth oral hygiene instructions, in-office fluoride applications, and at-home fluoride rinses, gels, and varnishes. An alternative approach, which possesses potential benefit regardless of patient compliance, includes the use of fluoride-releasing agents, such as composites, glass ionomers, sealants, and elastomeric ties.

Enamel decalcification or white spot formation, is a phenomenon occurring primarily on smooth enamel surfaces of teeth, notably within the gingival third of the crown. Demineralized enamel, the precursor to caries formation, can be attributed to fixed orthodontic appliances, and prolonged exposure to bacterial plaque. Bacterial plaque promotes the accumulation of acidic byproducts and demineralization that leads to successive changes in the optical properties of subsurface demineralized enamel. Progression to clinically detectable white spot lesions may occur as early as one month following the placement of orthodontic appliances.

Over the past thirty years, numerous studies have reported an increase in white spot lesions following orthodontic treatment. While a large portion of the non-orthodontically-treated population experiences some form of decalcification, orthodontically treated patient populations have shown both an increase in new lesions and an increase in the severity of preexisting enamel opacities. Approximately, 50 percent of orthodontically treated patients develop white spot lesions in one or more teeth, compared with only 24 percent in those not undergoing orthodontic treatment.

Appliance removal halts white spot formation, and further elimination of cariogenic factors through diligent oral hygiene efforts inactivates incipient lesions, which may undergo regression over time. Complete elimination of lesions is unlikely due to the rapid remineralization of the enamel surface with high concentration fluorides, which restrict passage of ions into the deeper, more affected layers. Therefore, immediate application of high concentration of fluoride is not recommended. Decreased enamel discolorations may occur with time due to further remineralization, but regression is primarily credited to gradual surface abrasion of tooth structure.

Such problems with enamel decalcification in orthodontic patients have influenced clinicians to search for a solution to orthodontic-associated demineralization. Because fluoride treatment immediately upon debonding is not advocated, clinicians have proposed fluoride treatment and fluoride-releasing materials at the commencement of therapy. Recommended solutions include oral hygiene instruction and reinforcement, fluoridated toothpastes, varnishes and mouthwashes, and fluoridated water supply. Lack of patient compliance hinders these efforts.

Two new anti-cavity toothpastes, Clinpro™ 5000 with 1.1% Sodium Fluoride and Clinpro™ Tooth Crème with 0.21% Sodium Fluoride, are currently available and have been shown in some initial case reports to be useful in the reduction of white spot lesions. Clinpro™ restores minerals and helps you produce saliva. Both the Clinpro™ products are advanced formulas containing an innovative tri-calcium phosphate ingredient. They are available exclusively from 3M ESPE. Clinpro™ contains fluoride as well as calcium and phosphate, which are components naturally found in saliva.

This proprietary formula successfully integrates these components, enhancing, rather than compromising, the product's performance. During the manufacturing process, a protective barrier is created around the calcium allowing it to coexist with the fluoride ions. Think of this as a bubble that transports the Tri-Calcium Phosphate to the teeth. As the toothpaste comes in contact with saliva during brushing, the barrier breaks down and makes the calcium, phosphate and fluoride readily available to the tooth. The tooth naturally absorbs these components, helping to prevent the initiation and further progression of demineralization and allowing remineralization to occur.

15. Participants (Screening and Selection)

a. How many participants are to be enrolled at UAB?90
If multi-center study, total number at all centers:____

b. Describe the characteristics of anticipated or planned participants.
Sex: both males and females
Race/Ethnicity: all races
Age: patients age 12-60 with adult dentition, i.e., permanent teeth (including adolescents)
Health status: medically fit and well

Note. If data from prior studies indicate differences between the genders or among racial/ethnic groups in the proposed research or if there are no data to support or to negate such differences, Phase 3 clinical trials will be required to include sufficient and appropriate entry of gender and racial/ethnic subgroups so that trends detected in the affected subgroups can be analyzed. If ethnic, racial, and gender estimates are not

included in the protocol, a clear rationale must be provided for exclusion of this information. If prior evidence indicates that the results will not show gender or racial differences, researchers are not required to use gender or race/ethnicity as selection criteria for study participants. They are, however, encouraged to include these groups. See Section II. Policy of the NIH POLICY AND GUIDELINES ON THE INCLUSION OF WOMEN AND MINORITIES AS SUBJECTS IN CLINICAL RESEARCH – Amended, October, 2001) for further details.

c. From what population(s) will the participants be derived?
patients coming to clinic for orthodontic treatment
Describe your ability to obtain access to the proposed population that will allow recruitment of the necessary number of participants:
orthodontic clinic
Describe the inclusion/exclusion criteria:
INCLUSION CRITERIA

1. Permanent dentition
2. Patients that in the opinion of the investigator will be compliant with the use of the paste
3. Patients who have not used extensive fluoride regimes
4. 12 years and older
5. Subjects must use a non-fluoridated toothpaste (such as Tom's of Maine) for a one-week period prior to starting this trial.

EXCLUSION CRITERIA

1. Any medical or dental condition that in the opinion of the investigator could impact study results during the expected length of the study.
2. Patient is currently using any investigational drug.
3. Patient plans to relocate or move within six months of enrollment.
4. Patients who have or are currently undergoing fluoride treatment for white spot lesions.
5. Patients with IgE Casein Allergy

d. If participants will comprise more than one group or stratification, describe each group (e.g., treatment/intervention, placebo, controls, sham treatment) **and** provide the number of participants anticipated in each group.

Three groups of 30 subjects (one group with Clinpro™ 5000, one group with MI-Paste Plus, and one group with Clinpro™ Tooth Crème) each will be evaluated as a protocol for the reduction of white spot lesions at the start of orthodontic treatment. Subjects will be recruited through the Orthodontic Postgraduate Clinic at the University of Alabama at Birmingham School of Dentistry.

In order to fully evaluate each of the products, the selected product will be brushed on for two minutes twice daily for 4 months. After brushing on the product, patients should not rinse their mouths with water. Rather, they should just expectorate (spit) so they don't clear out the actives from the product. Patient should also not eat or drink for 30 minutes following the treatment.

Subjects will be reviewed every 4 weeks. Subjects and study administrator will not know if the investigational paste or placebo is being administered. However, the PIs will know. Dr. Kau and Dr. Browne will randomly choose subjects by drawing individual slips of paper from an envelope on which 30 of each study product (i.e., Clinpro™ 5000, MI-Paste Plus, or Clinpro™ Tooth Crème) will be written. Each subject will receive product based upon the treatment type written on the paper selected by PIs.

e. Indicate which, if any, of the special populations listed below will be involved in the protocol. Include the Special Populations Review Form (SPRF) if indicated.

- ☐ Pregnant Women: Attach SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
- ☐ Fetuses: Attach SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
- ☐ Neonates/Nonviable Neonates: SPRF—Pregnant Women, Fetuses, Neonates/Nonviable Neonates
- ☐ Prisoners: Attach SPRF—Prisoners
- ☒ Minors (<19 years old): Attach SPRF—Minors
- ☒ Employees or students at institution where research conducted
- ☐ Persons who are temporarily decisionally impaired
- ☐ Persons who are permanently decisionally impaired (e.g., mentally retarded)
- ☐ Non-English Speakers

For each box checked, describe why the group is included **and** the additional protections provided to protect the rights and welfare of these participants who are vulnerable to coercion:____

f. List any persons other than those directly involved in the study who will be at risk. If none, enter "None":None

g. Describe the process (e.g., recruitment, chart review) that will be used to seek potential participants (e.g., individuals, records, specimens). Research recruitment by non-treating physicians/staff may require completion of Partial Waiver of Authorization for Recruitment/Screening. (See http://main.uab.edu/show.asp?durki=61981.)
All orthodontic patients who meet the inclusion criteria will be invited to participate.

h. If you will use recruitment materials (e.g., advertisements, flyers, letters) to reach potential participants, attach a copy of each item. If not, identify the source (e.g., databases) from which you will recruit participants.
No, clinic patients only.

i. Describe the procedures for screening potential participants.
All orthodontic patients who meet the inclusion criteria will be invited to participate.

16. Protocol Procedures, Methods, and Duration of the Study—in nontechnical language

a. Describe the study methodology that will affect the participants—particularly in regard to any inconvenience, danger, or discomfort.

We will require all patients a two weeks washout period, during which time we will give them very specific brushing instructions for using a non-fluoridated product such as Tom's of Maine toothpaste. These are the same instructions that we will require them to follow with whichever product that the patient will later be randomized to use in the trial, i.e. Clinpro™ 5000, Clinpro™ Tooth Crème, or MI-Paste Plus. This will ensure that all patients will use the same application technique, even though not all patients would be of the same level of potential decay. This washout period will last the same length of time for all patients, even though it will not begin simultaneously for all patients.

Patient will brush on randomized product for two minutes twice daily for 4 months. After brushing on the product, patients should not rinse their mouths with water. Rather, they should just expectorate (spit). Patient should also not eat or drink for 30 minutes following the treatment. No other inconvenience, danger, or discomfort is expected as a result of study methodology.

b. What is the probable length of time required for the entire study (i.e., recruitment through data analysis to study closure)?

16 weeks

c. What is the total amount of time each participant will be involved?
Subjects will be reviewed every 4 weeks. Subjects will be reviewed on four weekly intervals.

d. If different phases are involved, what is the duration of each phase in which the participants will be involved? If no phases are involved, enter "not applicable."
not applicable

e. List the procedures, the length of time each will take, and the frequency of repetition, and indicate whether each is done solely for research or would already be performed for treatment or diagnostic purposes (routine care) for the population. *Insert additional table rows as needed.*

Procedure	Length of Time Required of Participants	Frequency of Repetition	Research (Res) –OR- Routine Care
A caries risk assessment will be used to determine the caries risk of all patients enrolled into the study.	~10 minutes	once, at start of treatment	☐Res ☒Routine
Patient brushes on study paste at home.	2 minutes	twice daily	☒Res ☐Routine
Patients will be reviewed every 4 weeks		twice, every 4 weeks	☒Res ☐Routine
Patient answers Patient Satisfaction Questionnaire in UAB Orthodontic Clinic.	10-15 minutes	twice, at each follow-up visit	☒Res ☐Routine
Patients will be evaluated for reduction of white spot lesions.	~10 minutes	once, at end of treatment	☐Res ☒Routine

f. Will an interview script or questionnaire be used? ☐Yes ☒No
If Yes, attach a copy.

g. Will participants incur any costs as a result of their participation? ☐Yes ☒No
If Yes, describe the reason for and amount of each foreseeable cost.

_____

h. Will participants be compensated? ☒Yes ☐No
If Yes, complete i-v:
i. Type: (e.g., cash, check, gift card, merchandise):Visa gift card
ii. Amount or Value:$25.00
iii. Method (e.g., mail, at visit): one-time issuance per patient, at clinic visit
iv. Timing of Payments: (e.g., every visit, each month): upon completion of clinical trial
v. Maximum Amount of Payments per Participant:$25.00

17. Describe the potential benefits of the research.

You may or may not benefit directly from taking part in this study. Although white spot lesions may appear less noticeable and teeth may feel less sensitive to hot or cold temperatures, this is not guaranteed. You will not benefit financially from any commercial gains from sales of any product resulting from this study. Research carried out on your results may lead to the development of marketable procedures, and any benefit from the commercial products will remain with the sponsor.

18. Risks

a. List the known risks—physical, psychological, social, economic, and/or legal—that participants may encounter as a result of procedures required in this protocol. Do not list risks resulting from standard-of-care procedures. *Note: Risks included in this protocol document should be included in the written consent document.*

- Skin allergic reaction (such as hives, swelling of the face, lips, tongue and/or throat which may cause difficulty in breathing or swallowing, and if not treated promptly could become life-threatening) due to contact with the device or its components. The types of materials that may come into contact with the skin include polyurethane, polycarbonate, neoprene, nylon, and styrene-butadiene. No latex is included in the OrthoPulse™.
- If you are, or will be, using any medication, herbal or "natural" remedy, during the course of this study, please inform your study orthodontist immediately. Please check with the study orthodontist before you begin taking a new medication while in this study.
- Low level laser light exposure to the eye (if the Face Frame is not properly worn during the treatment). Do not stare directly at the light, and close your eyes when taking the headset on and off.
- By signing the Informed Consent, parent or guardian agrees to be present at (and monitor) all device applications of their child.

b. Estimate the frequency, severity, and reversibility of each risk listed.
upon contact, mild, discontinue contact

c. Is this a therapeutic study or intervention? ☒Yes ☐No
If Yes, complete the following items:
i. Describe the standard of care in the setting where the research will be conducted:____
ii. Describe any other alternative treatments or interventions: You may choose not participate in the Clinpro™/MI-Paste Plus™ study and still receive routine orthodontic treatment in the UAB Orthodontic Clinic.
iii. Describe any withholding of, delay in, or washout period for standard of care or alternative treatment that participants may be currently using: none

d. Do you foresee that participants might need additional medical or psychological resources as a result of the research procedures/interventions? ☐Yes ☒No
If Yes, describe the provisions that have been made to make these resources available.
____

e. Do the benefits or knowledge to be gained outweigh the risks to participants?
If No, provide justification for performing the research:____ ☒Yes ☐No

19. Precautions/Minimization of Risks (If study involves drugs or devices complete the Drug or Device Review Sheet and skip to question #20)

a. Describe precautions that will be taken to avoid risks and the means for monitoring to detect risks.

- Patient education and examination at regularly-scheduled follow-up visits
- By signing the Informed Consent, parent or guardian agrees to be present at (and monitor) all device applications of their child.

b. If hazards to an individual participant occur, describe (i) the criteria that will be used to decide whether that participant should be removed from the study; (ii) the procedure for removing such participants when necessary to protect their rights and welfare; and (iii)

any special procedures, precautions, or follow-up that will be used to ensure the safety of other currently enrolled participants.
All patients have the ability to stop using the product if adverse effects occur. This will be reported to PI who will stop the trial if necessary.

c. If hazards occur that might make the risks of participation outweigh the benefits for all participants, describe (i) the criteria that will be used to stop or end the entire study and (ii) any special procedures, precautions, or follow-up that will be used to ensure the safety of currently enrolled participants.
- Excessive whitening of teeth
- Inflammation of tissues

20. Informed Consent

a. Do you plan to obtain informed consent for this protocol? ☒**Yes** ☐**No**
If Yes, complete the items below.
If No, complete and include the Waiver of Informed Consent or Waiver of Authorization and Informed Consent, as applicable.

b. Do you plan to document informed consent for this protocol? ☒**Yes** ☐**No**
If Yes, complete the items below.
If No, complete the items below **and** include the Waiver of Informed Consent Documentation.

c. How will consent be obtained? by interview

d. Who will conduct the consent interview? PI or Research Coordinator

e. Who are the persons who will provide consent or permission? patients or their parents

f. What steps will be taken to minimize the possibility of coercion or undue influence?
Patients will neither be encouraged nor discouraged to participate in the trial.

g. What language will the prospective participant or the legally authorized representative understand? English only

h. What language will be used to obtain consent? English only

i. If any potential participants will be, or will have been, in a stressful, painful, or drugged condition before or during the consent process, describe the precautions proposed to overcome the effect of the condition on the consent process. If not, enter "no such effect."
no such effect

j. If any project-specific instruments will be used in the consenting process, such as flip charts or videos, describe the instrument(s) here, and provide a copy of each. If not, enter "not used."
not used

k. How long will participants have between the time they are told about the study and the time they must decide whether to enroll? If not 24 hours or more, describe the proposed time interval and why the 24-hour minimum is neither feasible nor practical. 30 minutes

21. Procedures to Protect Privacy

Describe the provisions included in the research to protect the privacy interests of participants (e.g., others will not overhear your conversation with potential participants, individuals will not be publicly identified or embarrassed).

Patients will be interviewed in a private room away from other patients and staff members.

22. Procedures to Maintain Confidentiality

a. Describe the manner and method for storing research data and maintaining confidentiality. If data will be stored electronically anywhere other than a server maintained centrally by UAB, identify the departmental and all computer systems used to store protocol-related data, and describe how access to that data will be limited to those with a need to know.
Paper patient records are stored in a locked file cabinet in a locked room. Electronic records are encrypted and password protected as required by standard UAB procedures.

b. Will any information derived from this study be given to any person, including the subject, or any group, including coordinating centers and sponsors? ☐Yes ☒No
If Yes, complete i-iii.

i. To whom will the information be given? ____
ii. What is the nature of the information? ____
iii. How will the information be identified, coded, etc.? ____

23. Additional Information

In the space below, provide any additional information that you believe may help the IRB review the proposed research, or enter "None."
None