Study Title: **Evaluation of 3M Clear Aligner for Correction of Class I, II and III Malocclusion Study**

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Clinical Study Protocol

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1. Background Information

1.1 Name, Description and Intended Use of the Product for Investigation

Orthodontic aligners have been commercially available since 1998 with the introduction of Invisalign® Aligners that are an aesthetic alternative for orthodontic treatment. 3M Oral Care Solutions Division plans to expand the orthodontic aesthetic solutions portfolio by offering customized 3M Clear Aligners for orthodontic treatment.

The 3M™ Clear Aligner System is a series of clear lightweight plastic appliances (aligners) indicated for the treatment of tooth malocclusions in patients with permanent dentition (i.e. all second molars). By utilizing a series of incremental tooth movements, (torque, tipping, rotation, bodily movements such as intrusion and extrusion) the 3M Clear Aligners sequentially re-position teeth by way of continuous gentle force.

The 3M Clear Aligner System may include attachments and/or buttons, which offer a solution for patients, who want an aesthetic treatment with a set of removable clear aligners that correct tooth malocclusions without the use of conventional wire and bracket orthodontic technology.

1.2 Risk/Benefit Summary

1.2.1 Risks

Listed below are the potential and known risks with wearing the 3M Clear Aligners:

- Gastrointestinal tract obstruction resulting from aligner fragments due to aligner breakage, attachment and button debond.
- Aspiration of 3M Clear Aligner fragments resulting from breakage, attachment, button debond.
- Aspiration of attachment or buttons resulting from breakage or bond failure.
- Choking due to 3M Clear Aligner fragments resulting from breakage.
- Choking due to attachment or buttons resulting from breakage or bond failure.
- Gingival tissue and teeth may become sore and tender after initial aligner placement and when placing each sequential 3M Clear Aligner.
- Speech may be affected when initially beginning treatment but should be minimized in 2 weeks after beginning aligner therapy.
- Gums, cheeks, and lips may be abraded or irritated by the 3M Clear Aligners, attachments or buttons
- Swollen and inflamed gums or tongue while wearing the 3M Clear Aligners.
- Enamel damage due to hard debris in aligner or due to removal of tight aligner.
- Staining of teeth due to poor hygiene, food debris in 3M Clear Aligner, or consumption of sugary liquids, or beverages that may cause stains on teeth, i.e. coffee, wine.

- Caries, decalcification periodontal disease and permanent stains may occur if consistent and proper oral hygiene such as brushing and flossing are not performed as recommended.
- Decalcification, and periodontal disease caused by eating and/or drinking sugary foods and beverages while wearing the 3M Clear Aligner.
- Tooth root damage due to tooth movement too fast or beyond bond while wearing the 3M Clear Aligner.
- The bite may change during the course of treatment resulting in temporary discomfort.
- The bite may require additional adjustments at the end of treatment.
- Temporary increase in salivation or dryness of mouth may occur.
- Temporal-mandibular joint (TMJ) pain, headaches or ear problems may occur.
- Existing dental restorations may become dislodged while removal of tight aligner.
- Failure to wear the appliance for the prescribed number of hours per day or in the prescribed order and/or not using the 3M Clear Aligner as directed may lengthen the treatment time and affect the final treatment outcome.
- Relapse of teeth after treatment due to the failure of not wearing the retainers.
- Attachment debonds which will require rebonding the attachment during an additional appointment
- Button debonds require rebonding the attachment during an additional appointment
- Aligners may become damaged
- Redness, swelling to gums, lips, due to sensitization to attachment composite material
- Toxicity from exposure to uncured attachment material.
- Cuts to gingiva, tongue, lips due to sharp or rough surface of attachment material.
- Respiratory tract irritation due to finishing/polishing dust or removal of attachment remnant material.

1.2.2 Benefits

The individual receives treatment for correcting tooth malocclusions, while wearing the 3M Clear Aligner instead of conventional wire and bracket orthodontic technology. Indirectly, subjects may benefit from the additional clinical attention.

1.3 Material Application

The subjects will undergo a target of up to 18 months of treatment to align the teeth to the planned target. The investigator will receive 6 sets of 3M Clear Aligners per shipment from 3M and will then provide each subject with 3 sets at each 6-week follow up appointment. The subject will wear the 3M Clear Aligners for at least 22 hours per day, with the exception of consumption of meals and beverages, with the exception of water, which can be consumed while wearing the aligners. During each 6-week period between follow up visits, subjects will wear

each set of 3M Clear Aligners for 2 weeks, in the order indicated per the Orthodontists treatment plan.

1.4 Good Clinical Practice (GCP) and Regulatory Requirements

The 3M™ Clear Aligner System is categorized as a Class II, medical device subject to 510(k) clearance. The 3M Aligner system has been cleared for use by the Federal Drug Administration. This study will be conducted in compliance with this protocol and Good Clinical Practice (GCP).

1.5 Study Population

The subject population for this study will be male and female subjects ≥ 14 years of age. There will be no attempt to enroll equal number of male and female subjects. Subjects who meet the inclusion and exclusion criteria will be asked to participate in the study. Up to a total of 180 subjects may be enrolled at up to 12 different clinical research sites, (up to 15 subjects per site).

2. Study Purpose and Objectives

The purpose of this study is to evaluate the safety and efficacy of the 3M Clear Aligners along with the use of attachments and/or buttons for the treatment of tooth malocclusions.

2.1 Primary Objective

The primary objective of this study is to evaluate the efficacy of 3M Clear Aligners to correct tooth malocclusions with the use of attachments and/or buttons, as determined by the amount of teeth movement and overall achievement goals of the treatment plan.

2.2 Secondary Objectives

The secondary objectives of this study are:

- Evaluate safety.
- Evaluate individual tooth movements per recommended treatment ranges.
- Evaluate length of treatment time for different malocclusions.
- Evaluate the use of attachments and attachment bond failures when used with 3M aligners.
- Evaluate orthodontist satisfaction with treatment outcome and use of 3M aligners.
- Evaluate orthodontist satisfaction with the Treatment Management Portal Software.
- Evaluate subject satisfaction with the overall treatment of the 3M Clear Aligners, especially regarding ease of insertion and removal, aesthetics (discoloration), ease of cleaning and subject compliance while wearing the aligners.
- Evaluate number of mid-course corrections or refinements needed.
- Evaluate digital scans to predict tooth movement for future product development.

3. Study Design

3.1 Study Type

This is a prospective, multi-center study with a targeted duration of 18 months, to assess the safety and efficacy of 3M Clear Aligners, with the use of attachments to correct teeth malocclusions.

3.2 Primary and Secondary Endpoints

3.2.1 Primary Endpoint

The primary endpoint is the percent of subjects who have achieved correction of tooth malocclusions with use of 3M Clear Aligners. The successful correction of the malocclusion will be based on the subject's achievement of the target setup or the treatment plan as judged by the Orthodontist.

3.2.2 Secondary Endpoints

- Safety of 3M Clear Aligners as evaluated by the number of unanticipated adverse events.
- Summary of individual tooth movement and total arch movements, for example, tooth rotations, tooth intrusions/extrusions, and arch space closures.
- Summary of treatment times for different tooth malocclusions
- Summary of the total number of aligners used, treatment duration and use of attachments, buttons, and bond failures.
- Percent satisfaction of orthodontists with treatment outcome.
- Percent satisfaction of orthodontist with the 3M Treatment Management Portal software.
- Percent satisfaction of subject with overall treatment when using 3M Clear Aligners, such as: (aligner comfort, pain during wear, ease of insertion, ease of removal, ease of cleaning and satisfaction with aesthetics).
- Summary of the number of mid-course corrections or refinements needed.

3.3 Randomization and Blinding

This is a single intervention schedule study so no randomization or blinding will occur. Subjects who meet the inclusion and exclusion criteria and are willing to sign an informed consent, will be asked to participate in the study.

3.4 Subject Identification

When a subject is considered eligible for entry into this study, the subject will be allocated to a subject identification number (subject ID number). The numbers will be sequential.

Subject identification will include the site number followed by the subject number. This number will be the unique identifier of the subject on the case report forms and written on each page of all other documentation relating to that subject.

A list of enrolled subjects and corresponding subject numbers will be maintained in the investigator's study file.

3.5 Study Materials and Labeling

3.5.1 Study Materials

3M Clear Aligners, attachment template including attachments will be provided by 3M.

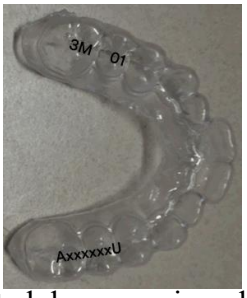
3M Clear Aligners
The 3M Clear Aligners are clear lightweight plastic appliances (aligners) indicated for the treatment of tooth malocclusions. 3M will provide 6 stages (12 weeks) of 3M Clear Aligners to site per shipment.

3M Attachment Template
The 3M Attachment Template is a lightweight plastic template used to create attachments on the subject's teeth.

3M Attachment Material
The 3M Attachment Materials are commercially available. The 3M Transbond XT and Transbond LV will be made available for Investigator use to create attachments, using the 3M Attachment Template.

Buttons
Investigator may use commercially available buttons for alignment, as indicated per treatment plan.

A picture of a 3M Clear Aligner is shown below:

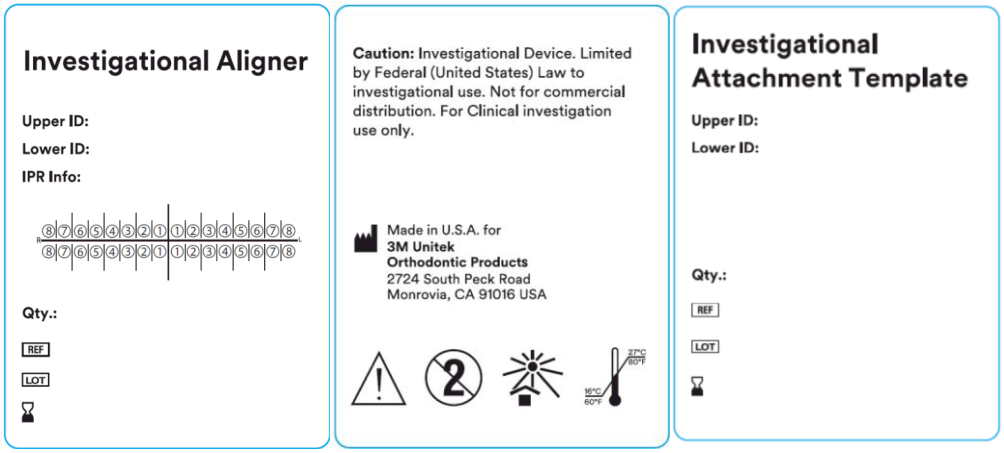


- Axxxxxx – 6 digit alpha-numeric order number
- U – Upper/Lower arch indicator
- 01 – indicates the stage number which will change as treatment progresses

3.5.2 Labeling

3M will label, package and ship the study materials to the clinical site. The aligners and aligner packaging used in the study will be labeled with the following minimum information:

- Medical Device
- *Order number – AxxxxxxABC*
- 3M Unitek Orthodontic Products
- Study material name or code designation
- Identifying lot
- Quantity of contents
- Include the following information as appropriate:
- Necessary caution statements (e.g. specific contraindications, hazards, adverse effects, interfering substances, devices or drugs, warnings and precautions that need to appear on the label for safe product use)
- Not for commercial distribution. For clinical use only.
- Storage conditions
- Expiration date



Material Label Statements
The 3M Clear Aligners and 3M Attachment Template are available for clinical use and has received Federal Drug Administration clearance.

3.6 Study Duration

The expected duration of subject participation may be 6 to 24 months, even though the maximum targeted duration is 18 months. The duration could be extended due to mid-course corrections or refinements, as determined by the Investigator. The subject is expected to attend study visits at 6-week intervals for the duration of the study. Study visits may range from a minimum of 7 to 18 scheduled visits, dependent on the duration indicated per the investigators treatment plan for each subject. Additional visits may be scheduled per Investigator discretion.

3.7 Study Termination/Subject Discontinuation

3.7.1 Study Termination

3M or the Investigator has the right to discontinue the study at any time for medical and/or administrative reasons, after mutual consultation, if possible.

The orthodontist, dentists or study sites have the right to discontinue this study at any time for safety and/or administrative reasons. If the study is discontinued prematurely, orthodontists, and subjects will be notified and proper documentation of the reason for discontinuation will be prepared. The IRB will be informed promptly and provided the reasons(s) for the termination or suspension by 3M.

3.7.2 Subject Discontinuation

The Investigator may discontinue individual subjects from the study at any time. Subjects may voluntarily withdraw from the study at any time. The Investigator will provide a written report on the appropriate CRF describing the reason for discontinuance and the date of discontinuance.

A subject will be discontinued from the study if any of the following occur:

- Subject fails to comply with instructions for wearing the 3M Clear Aligner as indicated per the Investigator treatment plan, for the duration required.
- Subject fails to show up at scheduled visits. Attempts will be made to schedule subjects and if they are not responsive, they may be discontinued.
- Subject elects to terminate participation in the study.
- Investigator elects to withdraw the subject (with written justifications about safety, noncompliance or for other safety reasons).
- Subject experiences a severe adverse reaction to the 3M Clear Aligner.
- Subject requires dental work that cannot wait until the end of the study.

Subjects who are withdrawn after wearing aligners will not be replaced. If possible, any procedures or assessments planned for the subject on withdrawal from the study should be performed when intention to withdraw the subject is announced

3.8 Material Accountability

Accountability and adequate inventory security will be maintained at all times.

- Investigator will maintain materials in a secure storage area, accessible only to authorized site personnel.
- Investigator will dispense study material only to enrolled subjects.
- Investigator will return all used 3M Clear Aligners to 3M after each subject's 6 week follow up visit within 1 week.
- Investigator will return all unused 3M Aligner System materials to 3M after subjects have completed all follow up visits.

The Principal Investigator or an authorized designee shall keep records documenting the receipt, use, and return of the 3M aligner system materials, which shall include:

- Date of receipt
- Identification of each 3M Clear Aligner; unique aligner identification and lot numbers
- Date of use
- Subject identification numbers
- Date on which the 3M Clear Aligners were returned to the 3M
- Date of return of unused, expired or malfunctioning 3M aligner system materials to 3M

3M will keep records to document shipment of 3M Clear Aligners to the clinical sites and all returned 3M Clear Aligners.

3.9 Randomization and Blinding

There will not be any randomization or blinding associated with this study, as it is a single intervention schedule. Subjects who meet the inclusion and exclusion criteria will be asked to participate in the study.

3.10 Source Data

Source documents are defined as the results of original observations and activities of a clinical investigation. Source documents will include, but are not limited to, paper copies of CRFs with original data, study progress notes, computer printouts, screening logs, laboratory notebooks, and recorded data from automated instruments. All source documents produced in this study will be maintained by the Investigator and made available for inspection by authorized persons. Paper CRFs will be the primary source documents for the study. All data will be directly recorded on the paper CRFs and later transferred to the electronic CRFs. Documentation may include, but are not limited to performance data, qualification criteria and any raw data generated for the study. The original signed informed consent form from each participating subject shall be filed in the Regulatory Folder and a copy provided to subject**.**

3.11 Protocol Modifications

3.11.1 Protocol Amendments

The party initiating an amendment must confirm it clearly in writing using the Amendment/Administrative Revision form. It must be signed and dated by 3M and, in the case of a significant amendment, the Investigator. A significant amendment means one that affects the safety, rights or welfare of subjects, the scope of the investigation or the scientific quality of the study.

3.11.2 Protocol Deviations

A deviation is a departure from the protocol that will likely affect the safety, rights or welfare of subjects, the scope of the investigation or the scientific quality of the study.

A protocol deviation is only for an individual subject. Protocol deviations are documented on a Protocol Deviation Form or appropriate CRF.

Deviations that potentially affect 1) subject safety, rights or welfare, 2) data integrity or 3) compromise the statistical analysis of the study require immediate communication to 3M. The Investigator must contact the 3M study monitor within 24 hours of occurrence.

A Protocol Deviation Form must be completed by the Investigator and include the type of deviation and a description of the circumstances surrounding the deviation. A copy is sent to the 3M study monitor within 24 hours of identifying the occurrence.

Deviations which are made to protect the life or physical well-being of a subject in an emergency must be reported to the IRB within 5 working days after 3M learns of the occurrence.

Any finding that is considered to have a significant impact on the study objectives or integrity of the study as assessed by the Principal Investigator will be reported to the 3M as soon as it is possible to do so.

3M Clear Aligners worn less than 22 hours per day will not be considered a protocol deviation, but will be recorded as non-compliance on the CRF.

4. Subject Selection

4.1 Subject Inclusion Criteria

Subjects to whom all of these conditions apply will be eligible to participate in this study:

1. Subject is at least 14 years of age.
2. Subject is willing and able to give informed consent.
3. Subject is willing to be digitally scanned at each 6-week visit, including after application of attachments.
4. Subject has a need for single or double arch orthodontic treatment with a target duration of 18 months or less.
5. Subject has good oral hygiene defined by the orthodontist.
6. Subject has only permanent dentition.

4.2 Subject Exclusion Criteria

Subjects to whom any of these conditions apply will be excluded from participating in this study:

1. Subject has skeletal discrepancies requiring surgery
2. Subject is undergoing active dental work
3. Subject has severe open bite > 2 mm
4. Subject has severe overjet > 4 mm
5. Subject has deep bite > 3 mm
6. Subject has over crowding per arch > 4 mm
7. Subject has dental prostheses/implants that will interfere with projected teeth movement
8. Subject is taking systemic steroid medication
9. Subject is taking Biphosphonates or any other medication for treatment of osteoporosis

4.3 Subject Informed Consent

The Investigator must ensure that written informed consent to participate in the investigation is obtained before including any individual as a subject in the investigation. The Investigator must provide the prospective subject or the representative sufficient opportunity to consider whether or not to participate, and minimize the possibility of coercion or undue influence. The process is designed to 1) give the subject all the information that they need, 2) ensure that the subject understands the information and 3) give the subject a chance to consider study participation. The process should permit the subject to ask questions and exchange information freely.

Specifically, the Investigator will explain to each subject all elements of informed consent as specified in 21 CFR 50.25 (Appendix 14). After the explanation, the subject or representative will voluntarily sign and date the consent form if they wish to participate in the study. A copy of the consent form must be provided to the subject. A signed and dated copy of the consent form must be maintained in the Investigator study documentation file at all times. The consent process and study participation, with date, must be documented in the patient record/chart.

For children under 18 years of age:
Prior to entering the study, the Investigator or qualified designee will explain to each legal parental custodian the nature of the study, its purpose, procedures, expected duration, and the benefits and risks involved in study participation. The study should also be explained to all subjects regardless of age to the fullest extent possible. Each legal parental custodian will be given an information and consent document and ample opportunity to ask questions. The legal parental custodian(s) will be informed of the subject's right to withdraw from the study at any time without prejudice. Subjects should also be given the opportunity to ask questions and be informed of their right to withdraw from the study. After this explanation and before any study-specific procedures have been performed, subjects may voluntarily assent to enroll in the study (the age of assent will be determined by the IRB, consistent with local laws, generally ≥7 years of age) and their legal parental custodian(s) may voluntarily sign and date an informed consent statement, thereby giving permission for their charges to enter the study. Prior to participation in

the study, the subject and their legal parental custodian(s) will receive a copy of the signed and dated written informed consent and assent forms and any other written information provided to the subject.

Written assent is generally not required of subjects <7 years of age due to maturation levels, depending on IRB policy and local laws. Their legal parental custodian(s) are responsible for evaluating the proposed study and providing written consent (permission) for their charges to enter the study. It is the Investigator's responsibility to ensure that the individual signing the informed consent document is the legal custodian for the subject. Impartial witness and/or Investigator signature and date will be added to the consent and assent documents if required by IRB policy.

Written informed consent or assent for each subject must be obtained before any study related procedures are performed.

4.4 Subject Authorization for Use and Disclosure of Protected Health Information

The Investigator must ensure that written authorization for use and disclosure of protected health information is obtained before including any individual as a subject in the investigation.

Specifically, the Investigator is to explain to each subject all elements of authorization as specified in 45 CFR 164.508. After the explanation, the subject or representative **must** voluntarily sign and date the authorization form if they wish to participate in the study. A copy of the authorization form must be provided to the subject. A signed and dated copy of the authorization form must be maintained in the Investigator study documentation file at all times and may be placed in the patient's medical record.

An authorization form may be combined with a consent form (i.e. compound authorization) if required by the IRB. All required elements for both informed consent and authorization must be included in a compound authorization.

4.4.1 Subject Revocation of Authorization to Use/Disclose Protected Health Information

In order to implement a valid revocation of authorization, the subject or their representative **must** make the request in writing to the Western Institutional Review Board. The revocation cannot stop the use or disclosure of information that has been collected prior to the revocation, is needed to ensure complete and accurate study results, is required by law or government regulation (e.g. reporting adverse events, etc.). Revocation of an authorization may not be used to withhold normal medical care from the subject, but may make the subject ineligible to receive the study treatment or care.

5. Treatment of Subjects

5.1 Schedule of Treatments

The 3M Aligner System includes a series of aligners that offer a solution for patients who want an aesthetic treatment with a set of removable aligners to correct tooth malocclusions without the use of conventional wire and bracket orthodontic technology. The 3M Clear Aligners are being studied in a manner consistent with their intended use.

The Principal Investigators will treat subjects requiring correction of tooth malocclusions using the 3M Clear Aligners with attachments and/or buttons as necessary for additional force applied to teeth or to help with tooth movement.

5.1.1 Subject Screening
Investigator will screen subjects for treatment of tooth malocclusion, as well as for study inclusion and exclusion criteria. If subject qualifies for the clinical study per the Investigator's examination, they will be provided with informed consent, per Good Clinical Practices. After subjects have signed the Informed Consent document, the investigator will determine whether subject's teeth should be cleaned by a hygienist before being scanned.

5.1.2 Initial Visit

- Determine subject eligibility.
- Consent eligible subjects.
- Investigator conduct initial examination and develop treatment plan.
- Generate initial digital scan of subject's teeth.
- Generate Pano-Ceph scan of subject's teeth.
- Generate Photos of subject’s teeth.
- For 3M™ True Definition Scanner upload the digital scan to 3M Study Lab 50005.
- For Itero users, retrieve the STL files from MyAligntech.com using OrthoCad export and save the STL scan files to local computer.
- For other scanner users, download the STL file to a local computer and upload the scan into the Treatment Management Portal website.
- Submit Treatment Management Portal order, with attached scan files, photographs and Pan-Ceph scans.
- Initial study documentation for each subject needs to be completed as follows:
  - Submit treatment order plan for each subject within 1 week of initial visit.
  - Upon receipt of final Target Set-up plan, approve or decline within 3 days.
  - Upon receipt of final Staging Set-up plan, approve or decline within 3 days.

Upon receipt of subject digital scan, Pano-Ceph scan, photos and Aligner specifications, 3M will generate (6 stages) 12 weeks of 3M Clear Aligners for subject. 3M Clear Aligners will be shipped to clinical site prior to subject's next scheduled 6-week follow up visit.

If timelines for treatment order plan and approvals for Target and Staging set-ups are not followed, this may impact 3M's ability to timely provide 3M Clear Aligners for subject follow-up visits.

5.1.3 Follow Up Visits

- Investigator will conduct follow up examination
- Generate digital scan of subject's teeth after application of attachments during first follow up visit and at each subsequent follow up visit.
- Investigator will assess 3M Clear Aligners for defects.
- Investigator will assess fit of 3M Clear Aligners.
- Investigator will assess seating and removal of 3M Clear Aligners.
- Investigator will inspect previously worn 3M Clear Aligners for damage and aesthetics.
- Investigator will assess subject’s teeth for missing attachments and/or buttons.
- Investigator will assess treatment progress.
- Investigator will assess soft tissue condition.
- Investigator will assess decision for mid-course correction or refinement.
- Investigator will provide subject with next 3 stages of 3M Clear Aligners.
  (Subjects will receive a total of three sets of 3M Clear Aligners (3 stages) at each 6-week visit.)
- Collect used 3M Clear Aligners from subject.
- Schedule subject's next 6-week study appointment.
- For 3M™ True Definition Scanner upload the digital scan to 3M Study Lab 50005.
- When using Itero, Trios or other scanners, retrieve the STL files and save the STL scan files to local computer. Scan will be provided to 3M.
- If applicable, submit new order for mid-course correction or refinement.
- Complete study documentation for each subject within 1 week of each visit.

5.1.4 Final Study Visit

- Investigator conducts final study examination.
- Generate digital scan of subject's teeth.
- Investigator will assess treatment progress.
- Investigator will assess soft tissue condition.
- Retainers will be provided to subject 2 – 3 weeks after final clinical study visit.
- Instruct subject to wear last set of 3M Clear Aligners until retainers are available.
- For 3M™ True Definition Scanner upload the digital scan to 3M Study Lab 50005.
- When using Itero, Trios or other scanners, retrieve the STL files and save the STL scan files to local computer. Scan will be provided to 3M.
- Log into Treatment Management Portal, go to the patient list and select the subject number.

- Select the Treatment Complete icon. This will inform manufacturing to use the final stage set-up model to manufacture three sets of retainers.
- Complete study documentation for each subject within 1 week of each visit.

5.1.5 Subject Instructions for Interim between 6-Week Follow-Up Visits
Subject will wear the 3M Clear Aligners for at least 22 hours per day with the exception of meals and beverages other than water.

- Subjects wear each of the (3) 3M Clear Aligner sets for two weeks, during the six-week period between study visits.

3M Clear Aligners Sets 1 - 3

3M Clear Aligner **Sets**		**Duration of Wear for Each Set (6 weeks total)**
Set # 1	Upper and Lower 3M Clear Aligners	2
Set # 2	Upper and Lower 3M Clear Aligners	2
Set # 3	Upper and Lower 3M Clear Aligners	2

- Subjects will receive 3 Stages of 3M Clear Aligners at every 6 week follow-up visit.

5.2 Study Procedures

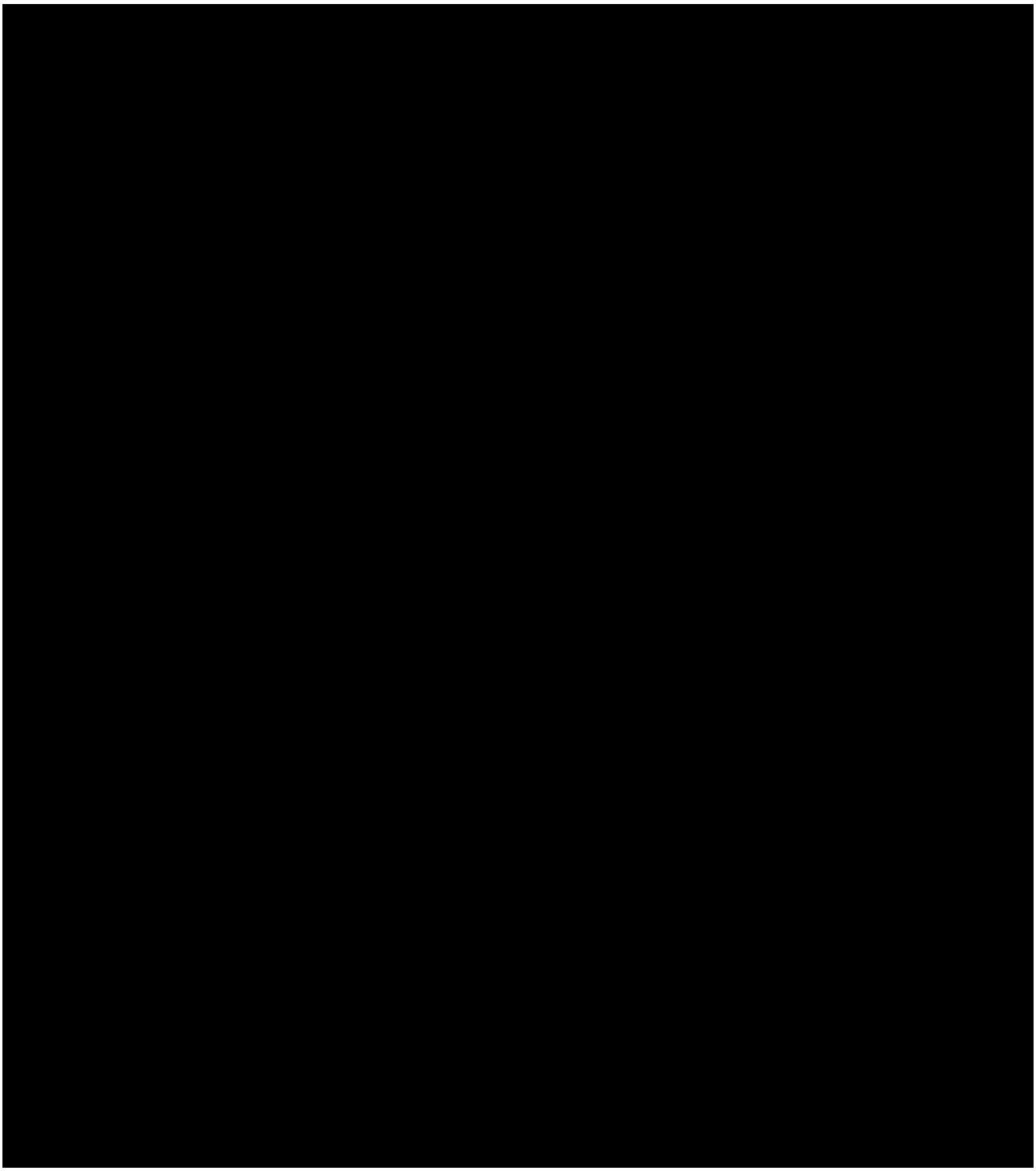
Instructions will be provided for the following procedures:

- Digital Scanning
- Submitting a 3M Clear Aligner order through 3M Treatment Management Portal.
- Target Set-Up and Staged Set-up Review and Approval
- Treatment with 3M Clear Aligners
- Instructions for Placing Attachments
- Patient Use and Care Instructions

5.2.1 Digital Scanning criteria:

- Subject will brush teeth prior to digital scan.
- Scan incisal edges and marginal ridges.
- Scan complete occlusal surfaces (no holes present).
- Scan inter-proximal spaces.
- Scan with clear gingival margin and 3-5 mm of lingual and buccal gingiva.
- Scan palatal rugae.

- Scan left and right bite scans to include 3 to 5 teeth in each scan, to ensure proper occlusion.
- Scan the terminal molars.
- **Do not scan anterior bite.**



[redacted]

5.2.4 Attachments

Based upon the investigator treatment plan, composite based attachments may be placed on the subject's teeth by the investigator using the 3M Attachment Template. Attachments are used to assist the 3M Clear Aligners in certain tooth movements or to engage the 3M Clear Aligners to directly apply pressure to certain teeth depending on the tooth size, shape and angulation.

Investigators may also place buttons they currently use in practice on the subjects teeth to assist with creating tooth movements and correcting occlusion in conjunction with attachments. Investigators may use buttons with elastics to assist in creating tooth movements such as rotation, intrusion, extrusion, translation. Investigators will bond the buttons onto the subjects' teeth according to the manufacturer's instructions. The investigator may modify the 3M Clear Aligner as needed, so that the 3M Clear Aligners fit around the buttons on the teeth.

Instructions for placing 3M attachments using the 3M Attachment Template can be found in the Aligner Attachment instructions for use. Instructions will cover the following:

- Tooth preparation
- Acid Etching
- Priming Teeth
- Bond the attachments and light cure
- Inspect the 3M Clear Aligners for any defects.
- Seat the 3M Clear Aligners to assess fit and adjust as needed.
- Assess the removal of the 3M Clear Aligners and adjust as needed.

For bonding buttons, follow the manufacturer instructions for use.

- Bond the buttons and modify the 3M Clear Aligners as needed to fit around the buttons.
- Inspect the 3M Clear Aligners for any defects.
- Seat the 3M Clear Aligners to assess fit and adjust as needed.
- Assess the removal of the 3M Clear Aligners and adjust as needed.

If the 3M Clear Aligners are not able to be seated and/or do not fit, contact 3M clinical study monitor.

5.2.5 Treatment with 3M Clear Aligners

After placement of the 3M Clear Aligners:

- Instruct subject on how to insert and remove the 3M Clear Aligners. Make sure subject is able to insert and remove 3M Clear Aligners before they leave the office. Investigator may provide auxiliaries to help subject with comfort while wearing 3M Clear Aligners and help with removal of the 3M Clear Aligners.
- Review and discuss the Patient Care and Use Instruction Sheet with subject.
- Allow each subject adequate time to ask questions.

- Provide subject with a 3M Clear Aligner case box.
- Inform the subject to return all 3M Clear Aligners in the original packaging along with the white box.
- In the event that a 3M Clear Aligner is lost or damaged, instruct subject to contact the office immediately.
- If a 3M Clear Aligner is lost or breaks within less than 7 days, instruct subject to begin wearing the previous set of 3M Clear Aligners.
- If a 3M Clear Aligner is lost or breaks after 7 days or more, instruct subject to begin wearing the next set of 3M Clear Aligners.
- Site will return all used and damaged 3M Clear Aligners to study 3M.
- Use shipping labels provided by 3M.
- Return 3M Clear Aligners in packaging provided and complete required packaging documentation.

If a 3M Clear Aligner is broken or lost, site should contact 3M clinical study monitor for replacement.

5.2.6 Mid-Course Correction or Refinement

In the event of a mid-course treatment correction or refinement, the following procedures should be followed:

- Generate digital scan of subject's teeth.
- Go to the Ordering Page in Treatment Management Portal and select option 6 to indicate that further treatment stages are cancelled.
- Submit new Treatment Management Portal order.
- After notification, review and approve both new target and stage set-ups.
- Corrected treatment will continue with 3M Clear Aligners identified as Tray # 1.

6. Subject Compliance

Routine office visits will be used to encourage subject compliance to study protocol. A 3M representative will monitor sites to oversee study documentation and compliance with study protocol.

7. Assessment of Efficacy

Efficacy of the 3M Clear Aligners for each subject will be based on the assessment by the investigator that teeth correction is progressing as expected at each orthodontic visit, and that the subject's teeth have reached the final target set-up by the end of treatment.

8. Assessment of Safety

8.1 Safety Parameters

The primary measures of safety will be evaluated by the incidence of adverse events reported during the study.

8.2 Adverse Events

The Investigator is responsible for identifying adverse events that occur to each subject throughout the study and follow-up period. An adverse event can occur at any time during the conduct of the study, in any phase of the study or after the study is completed. An adverse event can be identified by the Investigator or reported by the subject.

Note: The Federal Privacy Rule (HIPAA) specifically permits the use and disclosure of protected health information "without written authorization of the individual" when used for public health activities such as reporting adverse events, tracking FDA-related products, enabling recalls, repairs, replacements, lookbacks, or conducting post-market surveillance [45 CFR 164.512]. This use and disclosure is subject to the *minimum necessary* standard, i.e. "the minimum necessary to accomplish the intended use, disclosure, or request" [45 CFR 164.502(b)(1)].

Definitions

- Adverse event (AE) means any undesirable clinical occurrence in a subject whether or not it is considered to be device or drug related.

- Device-related adverse event (adverse device effect) is an AE considered by the Investigator to have a reasonable likelihood of being associated with the treatment device.

- Serious adverse device effect is a device effect that has a serious adverse effect on health or safety causing hospitalization or prolonged hospitalization, or is life threatening or causes death.

- Adverse drug experience is an AE that is considered by the Investigator to have a reasonable likelihood of being associated with the treatment drug.

- Serious adverse drug experience is an adverse drug experience that is fatal or life-threatening, requires inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant disability/incapacity, or results in a congenital anomaly/birth defect.

- An Unanticipated Adverse Device Effect (UADE) means any serious adverse effect on health or safety or any life-threatening problem or death caused by or associated with a

device, if that effect, problem or death was not previously identified in nature, severity or degree of incidence in the Protocol or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

All adverse events will be followed until they are resolved or for 30 days after the subject's participation in the study ends.

Recording and Reporting

The Investigator records each material-related adverse event on an Adverse Device Effect Record**.** Documentation includes the description, severity, seriousness, date of onset and resolution, relationship to the treatment material, action taken and outcome.

The Investigator must promptly report an adverse device effect to the 3M study monitor. If the adverse device effect is also considered by the Investigator to be serious and/or unanticipated, the Investigator must report it to the IRB as soon as possible and within IRB requirements.

A serious AE involving a non-3M commercialized product is reported to the 3M study monitor and IRB of record.

If a subject has no adverse device effect during the study, the absence of such must be recorded on the CRF.

9. Statistics

The primary efficacy dataset will include all subjects enrolled who have worn at least one set or first stage of 3M Clear Aligners in the study. The primary dataset will be referred to as the full analysis set or FAS.

A secondary efficacy dataset will be defined as the per protocol or PP dataset. This PP dataset will exclude subjects with major protocol deviations that will affect efficacy assessment of the 3M Clear Aligners. The major deviations that will lead to exclusion from the PP dataset will be fully documented and justified in the Statistical Analysis Plan (SAP) and/or pre-lock data meeting minutes. Two major protocol deviations that will lead to PP exclusion include significant non-compliance with aligner wear and not completing treatment due to non-treatment-related reasons (e.g. unexpectedly moving out of state). In general, a subject's failure to complete treatment due to strongly anchored teeth will be considered a treatment failure.

9.1 Statistical Methods

9.1.1 Analysis of Baseline and Demographic Characteristics

Subject demographics (age, gender) will be summarized for all enrolled subjects and for those considered evaluable for the primary endpoint. Individual subject malocclusions diagnosed at baseline or study enrollment will be summarized also.

9.1.2 Analysis of Primary Endpoint

The primary endpoint is the proportion of subjects achieving treatment success or attainment of teeth movements targets of the final set-up. It is possible for the final set-up to be modified mid-treatment or to be refined at the end of treatment, and thus success of the aligner with be based on the last or most relevant final set-up. Primary endpoint will be ascertained at the end of active 3M Clear Aligner wear (before retainer use). Subjects missing their primary endpoint assessment (e.g., subjects lost to follow-up) will be assumed to be treatment failures. The two-sided 95% confidence interval of this proportion will be computed using the Wilson score method. Documentation of subjects excluded from either the FAS or PP datasets for the computation of success rate will be justified and documented prior to datalock.

9.1.3 Analysis of Secondary endpoints

In general, the reported summary statistics for continuous measures will include number, mean, standard deviation, median and range. Reported summary statistics for categorical measures will include number and frequency.

Summaries of the overall percent completion or accuracy per subject will be summarized overall and for those categorized under treatment success or failure. Percent completion or percent accuracy will involve comparison of the final tooth positions relative to the planned or targeted positions against pre-treatment or baseline positions.

In addition, individual teeth movement and the malocclusions resolved in this study will be summarized as appropriate.

The secondary endpoints of treatment compliance, percent comfort and percent satisfaction will be summarized for various performance parameters.

Furthermore, summaries of attachment use, button use, and possible bond failures will be presented. In addition, occurrence of mid-course corrections and refinements will be summarized.

9.2 Sample Size Justification

The sample size for the study will be up to 180 subjects. The sample size was based on historical subject compliance and understanding of alignment procedures.

9.3 Interim analyses and Criteria for the Termination of the Study

At least one interim case study summary analysis may be conducted to examine the data regarding efficacy, safety and protocol deviations. A decision to stop the study may follow the interim summary analysis based on clinical results.

Given that no formal statistical testing will occur in this study, no allowance for alpha spending will be needed with any interim analysis.

10. Monitoring

3M, as sponsor of this study, is responsible for ensuring the proper conduct of the study with regard to protocol adherence and validity of the data recorded on the CRFs. 3M has therefore assigned a study monitor to this study. The monitor will be responsible for securing the compliance of the Principal Investigators to the signed agreement, the study Protocol and all applicable FDA regulations, guidelines and standards. The specific plans for monitoring will be detailed in the Monitoring Plan.

The assigned study monitor will conduct regular monitoring visits to the study site for which he/she is responsible. The Principal Investigator will allow the study monitor to inspect all Case Report Forms and the subject's clinic records and/or original medical records at these visits. These visits are for the purpose of verifying adherence to the Protocol and the completeness and accuracy of the data being entered on the Case Report Forms. The Investigator must make available the following for inspection and copying, in addition to any other documents deemed necessary for the integrity of the study data:

- Informed consent forms and HIPAA forms
- Protocol amendments, IRB/EC approval
- Protocol deviations
- Facilities at the study site
- Accounting of all 3M Clear Aligners
- Adverse events/adverse device effects that have been documented and reported

The progress of the study will be monitored by:

- Periodic on-site review
- Telephone communications
- Review of CRFs and source documents (e.g. patient hospital records, clinical charts, progress/doctor's notes, lab test results, x-rays, etc.)

Note: The Federal Privacy rule (HIPAA) specifically permits the use and disclosure of protected health information "to a person subject to the jurisdiction of the Food and Drug Administration (FDA) [e.g. study sponsor] with respect to an FDA-related product or activity for which that

person has responsibility, for the purpose of activities related to the quality, safety, or effectiveness of such FDA-regulated product or activity" [45 CFR 164.512(b)(1)(iii)].

11. Quality Control and Quality Assurance

3M is responsible for implementing and maintaining quality assurance and quality control systems through written standard operating procedures (SOPs) to ensure that this study is conducted and data are generated, documented and reported in compliance with the protocol, GCP and regulations cited in Section 1.5 of this protocol. Study monitoring is carried out to accomplish this.

12. Ethics

This study will be conducted in accordance with the principles that have their origin in the Declaration of Helsinki, 21 CFR 50 (Informed Consent) and 56 (IRBs).

The study will start only after approval of the protocol and consent form by the IRB. The approval letter or notice must contain the IRB name and identification number, meeting date, and sufficient information to identify the protocol and informed consent by name and number that were reviewed. 3M, prior to study initiation, must receive a copy of the IRB approval letter.

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

Confidentiality of subject data will be maintained at all times. Subject anonymity will be maintained and all documentation relating to a subject will be kept in a secure location.

13. Data Handling and Record Keeping

13.1 Study Personnel

Prior to study initiation, the Investigator must provide 3M with a signed investigator agreement (Statement of Investigator). The agreement contains pertinent investigator information (e.g. qualifications, experience, etc.) as well as the Investigator's commitment to conduct the study according to the protocol and all applicable state and federal regulations.

13.2 Pre-Study Documentation Requirements

Prior to study initiation, the Investigator must provide 3M with the following documents:

- Signed protocol including any amendments in place prior to study initiation
- Curriculum vitae for the Investigator and any co-investigators
- IRB approved waiver of consent and/or authorization
- IRB approved consent form.
- Authorization form
- IRB study approval letter
- IRB name, location and chairperson
- Financial Disclosure documents per 21 CFR 54
- Signed research agreement

13.3 Completion and Return of Case Report Forms

3M intends to use electronic data capture (eDC) software for this study. Sites will be trained on the eDC software prior to study enrollment. Each site will be provided with a manual, including instructions on how to complete the CRFs and how to make CRF corrections. Data may be recorded onto data collection sheets prior to data entry or may be entered directly into the eDC system. Once the forms are completed, the monitor will review the CRFs to assure accuracy and completeness. The Investigator must review and sign the CRFs for each subject in a timely fashion following completion.

13.4 Interim Report

Interim summaries of individual case reports may be written during the course of this study.

13.5 Final Report

3M will prepare and submit a Sponsor Final Report to all reviewing IRBs within 6 months after study completion or termination [see 21 CFR 812.150 (b)(7)].

13.6 Records, Reports and Retention Requirements

The Investigator will maintain study records for a minimum of 2 years following completion of the study. Records that must be maintained by the Investigator include, but are not restricted to:

- Signed study protocol, amendments, deviations
- IRB approval of protocol, consent form, authorization form* waiver of consent and/or authorization and amendments to any of these documents
- Applications to the IRB
- Signed consent and authorization forms
- Case report forms
- Adverse event reports
- Correspondence relating to the study
- Sponsor Final Report