Clinical Trial of Digitally Fabricated (3D Printed) Ankle Foot Orthoses
Frequently Asked Questions for Health Care Providers

The purpose of this resource is to share information about the Clinical Trial of Digitally Fabricated (3D Printed) Ankle Foot Orthoses . The questions in this FAQ sheet have been asked by medical providers. We have a separate Clinical Trial FAQ sheet for parents/guardians and a General FAQ sheet about AbilityMate. If this resource does not answer your questions please feel free to contact us: info@abilitymate.com

General Information about the Clinical Trial:

AbilityMate is sponsoring an observational study of 20-30 participants who will receive and wear Ankle Foot Orthoses (AFOs) manufactured through a digital process (3D Printing). The trial will be conducted in compliance with the trial protocol, GCP (Good Clinical Practice), ISO 14155 and all applicable regulatory requirements. The trial will have two key components:

1. Comparative laboratory testing of material properties - comparing material properties of the materials traditionally used to manufacture AFOs (thermoplastic polypropylene sheets) with the 3D Printed Nylon Material
2. Prescription, fitment and wearing of 3D Printed AFOs by participants - each participant will receive a custom prescribed and manufactured AFO and will wear it for 6 months.

AbilityMate decided to sponsor a trial so we could collect data about 3D Printing AFOs and use that knowledge to share and help Orthotists evolve their services. A clinical study is not a regulatory requirement in Australia and in the view of the TGA, it would have been possible for AbilityMate to make 3D printed AFOs available without the rigor of this study. We decided that it was in the best interests of the children and our future that we conduct a clinical study to validate the many potential benefits that 3D scanning and 3D printing can provide.

After completed a National Ethics Application Form (NEAF) the study has been issued a certificate of approval from Nepean Blue Mountains Local Health District Human Research Ethics Committee and issued this project ID: HREC/17/NEPEAN/35

For a small company, a considerable amount of investment has been made to conduct this clinical study. It will cost us more than $400,000. We have worked very hard fundraising and this study would not have been possible without the support of many generous volunteers, individuals funders and foundations.

For more specific information about AbilityMate we have created a separate FAQ 's about us. We are also in the process of creating an industry reference group, running Q&A webinars as well as attending industry conferences.

When will the Clinical Trial team engage with trial participants?

There are several touch-points throughout this study when the clinical trial team will engage with participants, parents and guardians. Below is a list of all planned engagements:

1. Recruitment (through various channels)
2. Phone screening with parents/guardians (Coordinator)
3. In-clinic consent, assessment and scan session (Investigator)
4. In-clinic fitting session (Investigator)
5. In-clinic follow up 2 weeks after fitment (Investigator)
6. Monthly phone call follow ups (Investigator)
7. At home diary study for parents at weekly intervals (reply-paid post)
8. In-clinic follow up after 6 months (Investigator)

AbilityMate (the sponsor) has no involvement in screening participants. AbilityMate also does not collect any information or study data about the participants such as biomechanical outcomes - this data is collected by the investigators. AbilityMate's 3D Modeller is required to collate study data about modeling and production times and has undergone training in Good Clinical Practice conducted by and ISO 14155 certified Clinical Trial consultancy group called Mobius Medical. The clinical trial team have signed disclaimers ensuring all data collected is true and accurate.

Where is the Clinical Trial taking place and who are the Investigators?

The study is being conducted at a clinic in Guildford, NSW, Australia (Korthotics).

The investigators are:
Merrick Smith - Senior Orthotist & Managing Director, Korthotics, Guildford
Vandeth Chhun - Clinical Orthotist, Northcott Equipment, North Parramatta

What are the primary & secondary endpoints of this Clinical Trial?

Primary

The primary endpoint of the trial is to explore whether AFOs manufactured through digital fabrication (3D printing & scanning) technology are a biomechanically viable alternative to traditionally manufactured AFOs for participants aged 2-8 years with physical disabilities.

Secondary

The secondary endpoints of the trial are to explore:

1. Whether 3D printed AFOs are equally as robust and safe (i.e. can withstand the same forces, have the same failure points) as traditionally manufactured AFOs when all materials undergo comparative mechanical testing
2. Whether the utilisation of 3D scanners reduces the distress experienced by participants and their families when being measured for an AFO, compared to traditional plaster casting methods
3. Whether Orthotists have a better experience with the new digital method compared with the traditional manufacturing method (including ease of use, cost and timeframes)
4. Whether 3D printed AFOs have the same biomechanical outcomes for children with disabilities as traditionally manufactured AFOs e.g. participants have the same functional and mobility outcomes when measured by gait analysis.

How are you recruiting for the study? How has it been advertised?

Recruitment for the study is being done through a number of channels including Cerebral Palsy Alliance, Northcott, AOPA's facebook page and distribution of flyers, social media and press releases. All recruitment materials have been approved by Nepean Blue Mountains Local Health District Human Research Ethics Committee (HREC). However some media releases (such as a recent Channel 9 News piece) were released without us being given an opportunity to review the content, and may not have accurately represented the facts or our views. We are working on ways to ensure this doesn't happen in the future.

If you would like to help us find applicants to the study that would be great.

Please contact Samantha Frain from Northcott Innovation on sam@northcottinnovation.com.au

How are the participants screened for this study?

The Trial Coordinator uses a checklist to ask several screening questions at the point of inquiry, at enrollment and these are checked again in person at the first appointment by the Investigator. The Trial Coordinator also receives a referral letter from a Doctor or Allied Health Professional that includes screening information.

How are you ensuring participants are not undergoing other interventions such as Botox?

The screening process mentioned above collects background information on previous interventions the child has had. In addition, the Orthotist further questions the parents and looks out for any signs of other interventions. However we are reliant to some degree on parents and health providers to provide accurate background information.

By excluding children who have had botox, you may be excluding the "stiffer" kids. Will the results therefore be biased?

We are including participants who have not received botox treatment for 9 months prior to the trial start date. If they have had botox less than 9 months and/or expected to receive botox treatment during the 7 month trial period they are unfortunately excluded. If botox treatment is needed during trial the participant can then withdraw. This is the case for the entire sample.

After consultation with our Investigators and other Orthotists that including children who are having botox treatment would biasly skew our results for the better. We are aware that botox treatment is a very effective for some children and positive results could potentially be a reflection of the botox rather than the trial AFO.

Who do participants require a referral from to be part of the study?

A healthcare practitioner that can prescribe AFOS. After consultation with our Investigators and other Orthotists it was bought to our attention that our protocol stated "For participants to be included in the trial a parent/guardian needs to provide a referral from an Allied Health Professional **(Physiotherapist/Occupational Therapist)**"

We are in the process of amending the protocol with the HREC to state "For participants to be included in the trial a parent/guardian needs to provide a referral from a relevant **Healthcare Practitioner or Allied Health Professional**

The protocol amendment is planned to be approved on 7th August 2017.

How will healthcare practitioners know if their patient is involved in the study?

We cannot inform other healthcare practitioners if their patient is involved in the study without parent/guardian consent. After consultation with our Investigators and other Orthotists it was brought to our attention that our trial could have this question in the consent process.

We are now amending the consent process with HREC to include a question asking permission for the parent/guardian if they consent to the clinical trial team making contact their relevant healthcare practitioner(s) e.g Orthtotist, Physiotherapist. If the parent/guardian consents then we can notify their healthcare practitioner(s). The protocol amendment is planned to be approved on 7th August 2017.

Will a child be excluded from the trial if they have already undergone 3D scanning and CAD (computer aided design) in the delivery of an AFO?

No they will not be excluded from the trial if they have undergone 3D scanning or CAD design - this will be the parent/guardian's decision.

We have a data collection process that asks parent/guardians if they have already undergone 3D scanning and CAD in the delivery of an AFO. This information is a baseline. We know that some parents may not fully inform us of the background and we hope to work more closely with their Orthotists if consent is granted, to ensure that their current treatment is being communicated.

Can you clarify the pathological selection criteria? There has been some confusion around definitive disability diagnosis and GMFCS score. Will the study only include children with Cerebral Palsy (CP)? Will children with Spina Bifida be included in the study?

After consultation with our Investigators and other Orthotists some confusion was brought to our attention and we have a protocol amendment in progress with the HREC. To clarify, yes the study will include participants with disabilities other than CP, including Spina Bifida. The criteria will state that a child needs to have a functional mobility score of GMFCS 1, 2 or equivalent.

The protocol also states that a child may be excluded if their medical condition is deemed high risk by the Investigator/prescribing Orthotists.

The protocol amendment is planned to be approved on 7th August 2017.

Will there be a control group? If not how will you make comparisons between 3D printed AFOs and thermoplastic AFOs?

During the trial design we considered the ethical and clinical implications of various forms of control groups. In defining the trial we engaged with our research ethics committee, health care practitioners and clinical trial experts. It was not considered ethical or clinically valid to have a control group of kids who receive either a thermoplastic AFO or a placebo AFO.
To make comparisons between 3D printed AFOs and thermoplastic AFOs we are conducting comparative laboratory testing to measure the physical properties of both.

Initial safety testing was done before the trial commenced, and we can share the results with you upon request. More in-depth testing, including ageing characteristics of the material are being done as part of the trial.

To evaluate biomechanical outcomes there are two Orthotists with extensive experience conducting assessments and evaluations of each child before and after wearing the AFO, including gait-analysis and the ISPO Lower Limb Assessment Template.

Methods of measurement include:

- Clinical observation and clinical assessment by both study Orthotists, utilising measurement tools such as goniometer and gait-analysis
- Feedback from other health professionals supporting the child e.g. physiotherapist
- Parent/guardian feedback
- Participant feedback (where appropriate)

A full description of all tests and measurements performed is included in the Trial Protocol. Up-to-date copies are available upon request.

Who is determining the design of the AFO? Will this potentially be different to their current design? How will you maintain consistency?

Two experienced Orthotists are involved in the trial as Investigators and so decide what design is appropriate for each participant. This reflects current practice with traditional manufacturing methods where clinical decisions regarding AFO design is made at the time of assessment of the client.

Who is modifying the AFOs through CAD? What sort of clinical training have they received?

We are testing a central fabrication service model, where the Orthotist specifies the modifications they require, and our highly skilled CAD modelling team then modifies the AFO specifically to the Orthotist's instructions.

To ensure that the AFO is designed exactly to the Orthotist's instruction, there are 5 points of approval and quality assurance where the Orthotist can see the AFO design and ensure it is as they require. Once approved by two Orthotists, the AFO design is then sent to be 3D Printed. Assembly and fitment is conducted by the Orthotists to check fit, design and comfort. During the clinical trial we also perform gait analysis on each patient before and after fitment of the trial AFO.

We have invested over $250,000 in state-of-the-art CAD design tools and automation processes to streamline the design process and ensure accuracy. In addition, our lead

CAD modeller Richard Reid is a thought-leader in the design engineering industry with over 30 years experience designing components for Boeing and Toyota. He is on the panel for various CAD/CAM ISO standards. He is also a lecturer at UNSW Faculty of Engineering.

Throughout the trial the Orthotists and CAD modelling team are creating a common vocabulary which will be part of the resources created throughout this trial.

It is important to note that the CAD modeller does not have any input on design decisions. They is essentially just following the Orthotists commands.

What will happen if an AFO is a poor fit or fails and needs to be re-made? How will these details be included in the study?

If the AFO is a poor fit it will not be released to the participant. It will be re-made and the participant's parent/guardian will be asked to come back for another fitting, as per current practice. If there is an issue such as AFO breakage or the participant grows out of it, a new AFO will be made and the trial can continue. Parents have been given emergency contact details to report adverse events such as breakages. As per Australian GCP (Good Clinical Practice) and ISO 14155 we are required to log all adverse events and report all serious adverse events with 24 hours.

The study records clinical and manufacturing details of each participant, whether the AFO fits or not, etc. Some of the items measured include:

- Time taken to prescribe AFO (handover to modeller)
- Time taken to design AFO according to Orthotist prescription
- Number of revisions pre-manufacturing
- Number of revisions post-manufacturing
- Cost of 3D printed AFO
- Turn-around time from print-ready to produced
- Total turnaround time (from start of scan to successful fitting, including modifications)
- Cost of delivering AFO to Orthotist's clinic
- Time taken by Orthotist to assemble AFO
- Cost of parts including straps, joints, padding etc
- Number of revisions post fitment

We have engaged an external Clinical Trial Consultancy (Mobius Medical) to independently monitor the trial and ensure all data is being captured and integrity maintained as per GCP (Good Clinical Practice) and ISO 14155.

How have you ensured that the new materials are safe to apply to participant's skin over long periods of time?

The material used is medical grade nylon, which is internationally certified as a biocompatible material and is routinely used worldwide for medical grade implants. In addition, the participants wear a sock like with any other thermoplastic AFOs. As we understand, sock wearing is standard practise.

Who is responsible if a device fails and injures the patient?

During the clinical trial, we (AbilityMate) as the sponsor are ultimately responsible if the device fails in such a way while being used as prescribed. If the device fails while being used outside of the prescribed areas the parent is responsible. We have indemnities and clinical trial insurance in place to protect the families, the Orthotists and AbilityMate.

Before we launch our central fabrication services we will have all legal requirements in place. If this is of interest to you we are happy to provide a more detailed upon request. To express interest in any future central fabrication services please email: info@abilitymate.com

What measures taken to minimise/avoid bias?

The following measures are taken to minimise bias:

1. Use of second Orthotist - a second Orthotist is involved in the trial to give a second opinion on all clinical decisions
2. Randomisation - participants in the trial will be randomly selected from applicants that meet the inclusion criteria
3. Educating all researchers on awareness of typical bias factors such as confirmation bias, leading question bias and the halo effect etc.
4. Excluding patients that have had botox 9 months prior to trial start date, or withdrawing any patients requiring botox during course of their trial period (7 months)
5. The trial will be conducted in accordance with Mobius Medical Pty Ltd (CRO) quality management system standard operating procedures (SOPs).
6. The sponsor will only have viewing rights on the database
7. The investigator(s) may be audited at any time.

How to respond to questions from parents regarding the trial and if you have any concerns with their 3D printed AFO?

Feel free to reference our supporting documentation and website to answer questions as needed. In addition you may contact the following people:

- For technology related questions or concerns please contact either Melissa Fuller or Johan du Plessis from AbilityMate on info@abillitymate.com

- For questions regarding recruitment and screening please contact Sam Frain from Northcott Innovation on sam@northcottinnovation.com.au

- For clinical enquiries contact:
  - Merrick Smith
    Phone: 02 8710 4183
    Mobile: 0402 138 387

  - Vandeth Chhun
    Phone: 02 9890 0950