TOEFX INC. – LIGHT THERAPY STUDY PROTOCOL

A Pilot Study Evaluating the Feasibility and Usability of ToeFX Light Therapy Device for Mild to Moderate Distal Subungual Onychomycosis (DSO) of the Toenail

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Protocol No:	TFX-LTS-001
Revision:	1.1
Revision date:	2022-11-22
Study Products:	ToeFX Light Therapy Device

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1.0 Protocol Summary

Title	A Pilot Study Evaluating the Feasibility and Usability of ToeFX Light Therapy Device for Mild to Moderate Distal Subungual Onychomycosis (DSO) of the Toenail
Short Title	ToeFX light therapy pilot
Methodology	Open label, prospective, multi-site, multi-investigator
Study Sites	Hamilton Foot Clinic 1508 Upper James St., Hamilton, ON L9B 1K3 Bruyere Foot Specialists 1661 Montreal Rd #1, Gloucester, ON K1J 9B7 Wilson Foot Clinic 2409 Walkers Line, Burlington, ON L7M 4K1
Number of Study Subjects	100 subjects
Diagnosis and Main Inclusion Criteria	Healthy males or females who meet the following criteria: • are between 18-75 years of age. • have a clinical diagnosis of mild to moderate DSO in the nail of at least one great toe, with 20% to 50% clinical involvement of the target toenail, without dermatophytomas or lunula (matrix) involvement, without lunular or proximal involvement. • exhibit positive mycology results (ie, KOH test and culture of a dermatophyte) from the target great toenail, confirming common dermatophytes such as *T. rubrum.* • are willing to abstain from any other treatment for onychomycosis for the duration of the pilot study.
Study Product and Planned Use	The ToeFX Light Therapy system is intended as a safe, effective and non-invasive treatment for nail fungus.

	This device will be used in accordance with the attached protocol. This study will be an open-label, prospective pilot study. The subjects will be 100 patients with mild to moderate onychomycosis. The purpose of the study is to establish the efficacy of the ToeFX device, which has shown compelling results in *in vitro* and *ex vivo* (cadaver) studies but has not been tested in patients.
Primary Endpoint	Technical Success: We will monitor (a) whether subjects attain 3 mm or more of clear nail growth post-treatment (b) whether subjects show mycological cure of their infection, as verified by culturing.
Secondary Endpoints	• Usability and form factor reported by clinicians • Satisfaction with the treatment reported by patients

2.0 Background: Clinical Need

According to a report published by the NCBI on January 14, 2015 ("Nail fungus: Overview"; Link: https://www.ncbi.nlm.nih.gov/books/NBK279547/), some 3 to 12% of the population is affected by toenfail fungus, with older populations more likely to be affected. Indeed, fungal infection of nails (onychomycosis) is among the most prevalent infectious diseases in humans. According to a communication released by the Ontario College of Physicians and Surgeons in September 2019, the cure rate for topical treatments is only 6-23% after 1 year. Even after 1 year of treatment, topical treatments have limited efficacy. Moreover, onychomycosis is cosmetically distressing.

Beyond efficacy issues, treatment options for onychomycosis come with certain risks. A three-to-six-month regimen of oral antifungals comes with hepatotoxicity risk and a host of drug interaction possibilities. Most notably, the azole antifungals inhibit the most prevalent and critical hepatic enzyme (CYP3A4) in drug metabolism. Despite these interaction risks, oral therapy is more effective and takes up to 75% less time to complete than topical therapy. Cure rates for oral therapy fall between 45% to 70%, and total remission occurs for 35% to 80% of patients. (Source: *Onychomycosis Treatment: Are Topical Therapies Worthwhile*? Article published in July 2016 in *Contemporary Clnic* by Daniel Holland, Pharm D. Link: https://contemporaryclinic.pharmacytimes.com/acute-care/onychomycosis-treatment-are-topical-therapies-worthwhile)

2.1 Device Overview (LED light source)

The core component of the device is an LED light source emitting at two wavelength ranges. These wavelengths are red light at 630-680 nm (primary wavelength) and blue light at 450-470 nm (ancillary wavelength). The light source transfers energy to the infected region of the nails to break down fungus cells.

The light source operates with an accessory photosensitizer formulation based on the well-known aniline dye "methylene blue". Methylene blue (MB) has been approved by Health Canada for several other indications, although not for the specific treatment of onychomycosis. In the ToeFX Light Therapy device, MB acts as a photosensitizer, mediating the transfer of energy from the red LED light source to the fungus. The MB concentration is 0.5%.

The mode of action is as follows: upon application of light, the photosensitizer molecule absorbs energy to form a short-lived excited state. The excited-state molecule rapidly transfers energy to surrounding oxygen to produce reactive oxygen species (ROS), which selectively disrupt the fungal cells. These ROS are short-lived and the reaction ceases immediately upon deactivation of the light.

The light device and photosensitizer formulation are used in conjunction. The formulation is painted onto the surface of the affected nail and allowed to penetrate into the nail bed for 10 to 15 minutes. Red light at an intensity of 200 mW/cm^2 is subsequently applied to the same area for 4 to 6 minutes. The nail may also be exposed to blue light at an intensity of 200 mW/cm^2. The blue light has no effect on the photosensitizer and is of secondary importance; however, several research groups have confirmed that exposure to mild blue light can have anti-inflammatory effects (Refer to Section 6.02, "Previous Studies").

The treatment is administered 12 times over the course of 1 year. The light device has an expected lifetime of several thousand hours and is designed to dissipate ambient heat.

2.2 Procedural workflow

A foot care clinician applies a photosensitizer topically to infected toenails; the toenails are then exposed to the ToeFX light source for about 15 minutes. The patient visits the clinic to repeat the process at intervals of two weeks.

Intended Users

User	**Qualifications**	**Role & Location during ToeFX treatment**	**Interaction with ToeFX system**
Chiropodist	- Doctor of Chiropody - Training in diagnosis and treatment of onychomycosis	- Assess severity of nail fungus and administer or supervise administration of treatment	- Deploys ToeFX system by administration of topical formulation - Positions ToeFX light source over the infected area -Removes the ToeFX light source at the treatment's end point.

Podiatrist	- Doctor of Podiatry - Training in diagnosis and treatment of onychomycosis	- Assess severity of nail fungus and administer or supervise administration of treatment	- Deploys ToeFX system by administration of topical formulation - Positions ToeFX light source over the infected area -Removes the ToeFX light source at the treatment's end point.
Physician assistant	- Bachelor of Health Sciences (Physician Assistant specialization) -Training supporting foot care clinicians	- Assist with administration of ToeFX treatment - Collection of data, taking photographs of affected area	- May position light source over affected area and/or remove light source upon conclusion of the treatment.

Operating Environment
The ToeFX system is intended for use in any room in which standard foot care treatments are routinely administered.

3.0 Study Objectives

This study will be an open-label, prospective pilot study. The subjects will be 100 patients who suffer from DSO. The efficacy of photodynamic therapy for treatment of onychomycosis has been demonstrated in the literature. The purpose of the study is to establish the efficacy of the specific ToeFX device, which has shown compelling results in *in vitro* and *ex vivo* (cadaver) studies but has not been tested in patients. Specifically, we wish to:

1. Determine the safety and efficacy of ToeFX photodynamic therapy in the treatment of distal subungual onychomycosis of the toenail.
2. Determine the number of treatments required to clear the nail and to cure the fungus.
3. Finalize the treatment protocol, device design and user interface.
4. Test re-infection or recurrence of fungus post-treatment.

3.1 Overview of Study

Definition of distal subungual onychomycosis (DSO)
This type of onychomycosis is the most common clinical presentation, in which the distal nail plate is separated from the nail bed. This infection presents as nails with normal surface texture and thickness but variable "bays" of white nail that extend from the distal nail tip proximally into

the area of the nail bed. This form has been the cornerstone of antifungal drug studies. Since it generally does not involve the nail matrix, it is more amenable to improvement in clinical appearance than some other forms. In this trial only mild to moderate DSO cases will be included using the Onychomycosis Severity Index (OSI). An OSI score is obtained by multiplying the score for the area of involvement (range, 0-5) by the score for the proximity of disease to the matrix (range, 1-5).

A clinician or delegate will:
• Take representative before and after photos of nail/s prior to treatment.
• Provide a description of the treatment protocol used, including any adjunctive interventions such as topical antifungal products or debridement.
• Record occurrences and frequency of any adverse events.
• Prepare a table summarizing the percent complete responders, partial responders (which may be further stratified), and non-responders.
• Ensure that fungal species are assessed.
• Ensure that clinical presentations of onychomycosis are assessed (e.g., DSO).

3.2 Study Design

Study Type:	Interventional (clinical trial)
Actual Enrollment:	100 participants
Masking:	None (Open Label)
Primary Purpose:	Treatment
Study Start Date:	Immediately upon approval by Health Canada

Arm	**Intervention/treatment**
Arm 1 Red light only	Core technology. Formulation and red light only. Apply photosensitizer; allow to penetrate for 15 minutes; apply red light for 15 minutes.
Arm 2 Red and blue light	Apply photosensitizer; place foot under blue light and allow to penetrate for 15 minutes. Apply red light for 15 minutes.

Arm 1 will test the core technology of the ToeFX system; this study reproduces protocols described in the literature (see 'Previous Studies' in Section 6.02). Arm 2 pairs the core technology with application of blue light. After application of the formulation, the nail is exposed to blue light at a wavelength of 450-470 nm and an intensity of 200 mW/cm^2. The blue light has no effect on the photosensitizer; however, several research groups have confirmed that exposure to mild blue light can have anti-inflammatory effects that would improve patient

outcomes (see 'Previous Studies' in Section 6.02). We will assess whether inclusion of blue light in the protocol affects the clinical outcome.

Debridement should be done prior to each treatment. Debridement should not be carried out more proximally than the most proximal margin of the dystrophic nail, as this can interfere with assessment of clear nail area attributable to the device intervention. Clinician should debride the nail and apply the photosensitizer formula and let it penetrate for 15 minutes, then if applicable apply the blue light (450-470 nm). Apply the red light (640 nm) for 15 minutes. The treatment is administered 12 times over the course of 1 year.

3.3 Control

Our study cohort will be compared to known values published in a large multicenter trial of the topical solution Jublia (manufactured by Valeant). Jublia is a once-daily treatment of 10% w/w efinaconazole for the treatment of onychomycosis. Jublia showed a complete cure rate of 15-18% in a study of two groups of 800 patients.

We will follow the inclusion and exclusion criteria defined in the Jublia trial. Patients in the Jublia study showed 20% to 50% clinical involvement of the area of the target great toenail, without dermatophytomas or lunula (matrix) involvement. Patients had positive dermatophyte culture and positive potassium hydroxide (KOH) examination from the target toenail and were not excluded for concomitant *Candida* infection. Patients were assessed for clear nail.

Based on previously published studies of photodynamic therapy for onychomycosis, we expect to observe a complete cure rate on the order of 50-80%. Given the large difference in the observed cure rate for Jublia and the anticipated cure rate for the ToeFX Light Therapy device, a sample size of 100 patients is adequate to establish statistical significance of our results.

3.4 Outcome Measures

Clear nail: The specifications for clear nail are described below. The 95% one-sided confidence interval (i.e., lower bound only) around the observed response rate as described below should be ≥50%.

We will monitor whether subjects attain 3 mm or more of clear nail growth post-treatment. We will verify by taking a photograph prior to every treatment to assess the change in millimeters (mm) of clear nail bed. Millimeters (mm) of clear nail from the base of the toenail will be determined from digital photographs of the toenail and verified via software. The change in mm of clear nail bed will be calculated as the difference in mm of clear nail bed from baseline measurement to the measurement at the end of the procedure administration phase.

An increase in mm of clear nail between the two measurement points indicates that the toenail has improved and is positive for study success. A decrease in mm of clear nail between the two measurement points indicates that the toenail has worsened and is negative for study success.

Individual toenail success criterion is defined as 3 millimeter (mm) or more of clear nail growth as evaluated relative to baseline.

Length of the unaffected part of the target nail is measured in millimeters along the midpoint from the nail fold to the proximal border of the affected part (lowest point affected) along the midpoint of the target nail. Change from Baseline is: (Baseline value subtracted from 6-month treatment value). P-value shall be based on analysis of variance (ANOVA) with treatment and pooled center. Statistics will be provided for the adjusted least square mean.

To ensure adequate photographic quality and to maximize our ability to compare photographs across timepoints and across subjects, a standardized photography protocol will be put in place. Photographs shall be of high quality and high resolution. An internal scale (e.g. ruler) will be included in all images to allow objective measurement of millimeters of clear nail regardless of magnification of the image.

Mycology: Among toenails which are deemed responders based on the "clear nail" criteria, we will also assess for negative mycology (negative stain with concurrent negative culture, or two negative cultures from the same nail).

Follow-up: The goal of treatments for onychomycosis is elimination of the fungal organism and full clearance of the nail. Follow-up for this indication should be based on the anticipated time for complete nail regrowth, which is approximately 6 months. Longer follow-up times will be helpful for assessing recurrence rates. To control for loss of subjects who do not exhibit the desired visual outcome, subjects who drop out or are lost to follow-up will be considered as treatment failures for this indication.

3.5 Eligibility, Inclusion and Exclusion Criteria

Eligibility Criteria

Ages Eligible for Study:	18 Years to 75 Years (Adult, Older Adult)
Sexes Eligible for Study:	All
Accepts:	Persons with a clinical diagnosis of mild to moderate DSO

Inclusion Criteria

We are seeking otherwise healthy males or females who meet the following criteria:

- are between 18-75 years of age.
- have a clinical diagnosis of mild to moderate DSO in the nail of at least one great toe, with 20% to 50% clinical involvement of the target toenail, without dermatophytomas or lunula (matrix) involvement, without lunular or proximal involvement.
- exhibit positive mycology results (i.e., KOH test and culture of a dermatophyte) from the target great toenail, confirming common dermatophytes such as *T. rubrum.*

- are willing to refrain from using polish or other medication on treated toenails or on the skin immediately adjacent to the toenails during the treatment period unless directed to do so by the investigator.
- are willing to refrain from using topical steroids or topical antifungals on toenails or the skin immediately adjacent to the toenails or systemic antifungals for the duration of the study.
- are willing to provide signed and dated written voluntary informed consent in English before any protocol-specific procedures are performed.
- are able to complete the study and comply with study instructions.

Exclusion Criteria

The following populations are excluded from the study:

- patients with glucose-6 phosphate dehydrogenase (G6PD) deficiency or hypersensitivity/allergies to methylene blue.
- females who are pregnant, plan to become pregnant during the study, or are nursing a child.
    - As the effect on an unborn child is unknown, all female research participants of childbearing potential must take a urine pregnancy test at screening and every 3 months (12 weeks) for the duration of the Study.
    - Hormonal methods and/or IUD must be in use at least 30 days prior to first Study intervention; barrier methods must be in use at least 14 days prior to Study intervention; vasectomy must be completed 3 months prior to first Study intervention; or in the alternative a 0 sperm count will suffice.
- persons who are hypersensitive to topical creams, ointments, medications, or surfactants.
- persons who have received systemic antifungal therapy for any reason within 3 months, or topical antifungal therapy on the toenails or skin immediately adjacent to the toenails within 3 weeks prior to the start of the study.
- persons who have received an investigational drug within 4 weeks of the first dose of study product, or who are scheduled to receive an investigational drug other than the study product during the study.
- persons who have participated in a clinical trial for the systemic treatment of onychomycosis of the toenails within 6 months prior to the first dose of study product.
- persons who are not prepared to give up use of any nail cosmetic products for the duration of the study.
- persons who have any known immunodeficiency or history of malignancy in the last 4 years, excluding nonmelanoma skin cancer.
- persons currently suffering from any disease or condition, that could include abnormal laboratory tests, and/or who are currently using medication which in the opinion of the investigator may affect the evaluation of the study product or place the subject at undue risk.

- persons with psoriasis, lichen planus, or other medical conditions known to induce nail changes, other abnormalities or can causes of nail breakdown that can predispose to secondary fungal infection. Trauma from ill-fitting shoes, running, or overly aggressive nail care can also induce changes visually indistinguishable from onychomycosis that could result in a clinically abnormal toenail.
- persons with a history of any condition that could possibly affect absorption of drug (e.g., gastrectomy), uncontrolled diabetes, clinically significant peripheral vascular disease or peripheral circulatory impairment, or has had any major illness within 30 days prior to the screening examination.
- persons with a history of drug, prescription medicine, or alcohol abuse within the past 2 years.
- smokers.

3.6 Data Analysis

- Descriptive statistical analysis to analyze degree of response (e.g., complete response or clearing, >75% clear, 50-75% clear).
- Increase in clear nail at each timepoint of evaluation after the last treatment
- Increase in clear nail as a function of the number of treatments

To evaluate the overall response rates, we plan to ensure that the study report be presented in a tiered fashion, citing the success rate for the subjects exhibiting mycological cure concurrent with clear nail, with separate presentation of the data for subjects exhibiting mycological cure with residual nail dystrophy.

4.0 Study Procedures

4.1 Patient Recruitment and Screening

Potential study subjects will be identified by the co-investigators or any sub-investigators. It is anticipated that surgical consults will be the primary source of study candidates. Clinicians will ask patients who present with onychomycosis if they are interested in participating in the research trial; those who are interested will be assessed by the clinician for their compatibility with the inclusion/exclusion criteria. Patients that meet all criteria will be asked to submit a nail sample for mycological culturing. This initial review of existing patient information may be performed prior to subject consent; however, no protocol-driven tests or procedures may be performed until after informed consent has been obtained. If the subject shows positive mycology, he/she will be contacted via phone within 2 weeks and asked to sign an informed consent form in person, where a clinician will be present to answer any questions. If the patient is satisfied and has no questions, the treatments may commence at the clinic during the same visit. Research participants will remain in the study for one year.

For the occasional non-English speaking study participant, an on-site translator will be provided at the clinic at the expense of the Sponsor. Informed consent will be treated as an ongoing

process throughout a study. For those who understand English but cannot read, talk, or write, the investigator will provide the necessary support to ensure the subject's ongoing comprehension of new information that may become available during the study.

4.2 Informed Consent

Consent shall be obtained in accordance with Canada's Medical Device Regulations section 81(k)(ii) and the Tri-Council Policy Statement – Ethical Conduct for Research Involving Humans (TCPS2) and World Medical Association Declaration of Helsinki – Ethical Principles for Medical Research Involving Human Participants. Potential subjects must be informed as to the purpose of the study and the potential risks and benefits known or that can be reasonably predicted or expected as described in the written consent form. The patient shall have sufficient opportunity to consider participation in the study; consent forms shall be written in English. A patient cannot be led to believe that they are waiving their rights as a subject or the liability of the sponsor or investigator. Patients are then invited to sign and date the consent form, indicating their consent for enrollment (investigators may not date the consent form on the patient's behalf.) Once a patient has signed and dated the consent form, they are considered a subject enrolled in the study.

The person administering the consent signs and dates the consent form to indicate that the purpose, risk and benefits of the study were explained to the subject/caregiver and their signatures witnessed. Only study personnel who have been delegated by the Principal Investigator or Co-Investigators to perform this task may obtain informed consent and sign the consent forms.

The investigators will retain the original copy of the consent forms, signed and dated by the subject/caregiver, in the Investigator's Study File. A duplicate copy shall be provided to the subject.

4.3 Identification and Enrollment Log

Subjects who have signed the consent form will be given a unique subject number that shall be used to identify the subject on all study related documents. The Enrollment Log relates the subject number to the full name, address, telephone number and any other pertinent subject information. Once assigned a subject number, the investigator shall enter the remaining subject identification information into the log. This log is the primary way in which the subject identification is correlated to the actual identity of the subject. The Enrollment Log will be kept in a secure location with restricted access to only study staff, ensuring confidentiality is strictly maintained.

4.4 Subject Withdrawal

Subjects may be withdrawn from the study for any of the following reasons:

1. Subject's choice to withdraw their consent to participate. Any participant has the right to withdraw from the study at any time and for any reasons without prejudice to future medical care by the physician or the institution.
2. Investigator's choice to withdraw the subject from the study. An investigator may choose to withdraw a subject from the study due to changes to their medical condition which could interfere with their participation or if the study may interfere with their prompt and effective treatment.
3. Study termination for either administrative or safety reasons.

For participants who withdraw their consent for study participation, the Investigator will complete the "Subject Withdrawal" and no additional data will be collected after the date of their discontinuation.

5.0 Safety and Adverse Events

Although this is a low risk device, all adverse events related to such procedures should be reported by type, severity, duration, outcome, and relationship to the device or procedure in order to develop an accurate understanding of the risks and benefits of these procedures.

6.0 Study Management

As the study sponsor, ToeFX Inc. has the overall responsibility for the conduct of the study according to Canada's Medical Device Regulations Part 3, E6 Good Clinical Practice Consolidated Guidance, ICH, 1997), ISO 14155: Part 1 and 2, the Declaration of Helsinki, Medical Device Directive, Annex X, Health Canada, and all applicable local regulatory requirements. For this study, ToeFX Inc. will have certain direct responsibilities and will delegate other responsibilities to appropriate contract consultants. Together, ToeFX Inc. and their consultants will ensure that the study is conducted according to all applicable regulations. All personnel to participate in the conduct of this clinical trial will be qualified by training, education and/or experience to perform his or her respective tasks.

NOTE: A complete list of participating investigators will be maintained and will be available upon request.

6.1 Investigator Responsibilities

Responsibilities of the Investigator include, but are not limited to:

1. Ensuring that all personnel assisting with the clinical trial are adequately informed and understand their trial-related duties and functions
2. Obtain informed consents of subjects.
3. Permit sponsor or designated consultant to inspect facilities and records.
4. Maintain medical histories of subjects.
5. Enroll subjects, execute the study, transcribe data from source documents to case report forms, and conduct study in accordance with protocol.
6. Submit progress reports, final reports and any adverse events to the sponsor.

6.2 Sponsor Responsibilities

ToeFX Inc. is the Sponsor of this study; responsibilities include but are not limited to:

1. Selecting qualified investigators (qualifications will be documented by curriculum vitae)
2. Providing investigators with the information necessary to conduct the investigation properly
3. Providing appropriate training to the clinical site and all study personnel, as necessary
4. Documenting training where appropriate
5. Providing the devices to qualified investigators
6. Reporting and investigating unanticipated, device-related adverse events
7. Obtaining signed Investigator Agreement for each investigator prior to their participation in the study
8. Retaining records for at least 3 years following completion of this study.

6.3 Protocol Deviations

A protocol deviation is defined as any study action taken by the clinical Investigator or site personnel in conflict with the Study Protocol. Investigators must make every effort to follow the protocol except where necessary to protect the life or physical well being of a subject in an emergency. All deviations from the protocol will be reported on the appropriate Deviations Log.

Deviations must be reported to the Sponsor within a reasonable time frame. Subject specific deviations will be reported on the Deviations Log. Non-subject specific deviations, (e.g. unauthorized use of an investigational device outside the study, etc.), will be reported to the Principal Investigator.

6.4 Study Review Plan

The study will be reviewed every 30-45 days by the principal investigator and the sponsor to ensure that applicable regulations are followed. This is to ensure that each person involved in the study administration carries out the required duties.

6.5 Ethical Considerations

The rights, safety and well-being of clinical investigation subjects shall be protected consistent with the ethical principles laid down in the Declaration of Helsinki. This shall be understood, observed and applied at every step in this clinical investigation.

It is expected that all parties will share in the responsibility for ethical conduct in accordance with their respective roles in the investigation. The Sponsor and the Investigator(s) shall avoid improper influence or inducement of the subject, monitor, the clinical investigator(s) or other parties participating in or contributing to the clinical investigation.

6.5.1 Protection of Subject Confidentiality

At all times throughout the clinical investigation, confidentiality will be observed by all parties involved. All data shall be secured against unauthorized access. Privacy and confidentiality of information about each subject shall be preserved in study reports and in any publication. Each subject participating in this study will be assigned a unique identifier.

The Investigator will maintain a confidential subject list identifying all enrolled subjects (Enrollment Log). This list will contain the assigned subject's unique identifier and name. The Investigator bears responsibility for keeping this list confidential. This list will not be provided to the study sponsor and is only to be used at the study center.

Any source documents copied for monitoring purposes by the Sponsor will be identified by using the assigned subject's unique identifier in an effort to protect subject confidentiality.

6.5.2 Compensation and Study funding

Patients will be compensated for their time, parking expenses and any other costs incurred by consequence of their participation in the trial with $200 paid in two instalments at week 25 and week 50 of the 52-week study. The study is funded by ToeFX Inc., with in-kind support of donated time and clinic space from the principal investigator.

6.6 Final Report

A final report will be completed, even if the study is prematurely terminated. At the conclusion of the trial, an abstract reporting the results may be prepared and will be presented at a major meeting(s). A manuscript may also be prepared for publication in a reputable scientific journal.

7.0 Study Close-out

7.1 Close-out

A close-out visit will be conducted by the Sponsor or its monitor within 45 days of receipt of the last case report form.

7.2 Record Storage and Retention

The Clinical Site and the Sponsor shall retain copies of all study data and documentation for a minimum of 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or at least 2 years have elapsed since the formal discontinuation of clinical development. The Sponsor will notify the site of the planned marketing application and clinical development timelines with regards to record storage and retention. If the lead site investigator retires, relocates, or for other reasons

withdraws from the responsibility of keeping the study records, custody shall be transferred to a person who will accept that responsibility or to ToeFX Inc.

7.3 Discontinuation of Study

ToeFX Inc. reserves the right to discontinue any study for business or ethical reasons at any time, such as but not limited to, a decision to discontinue further clinical investigations with the test article, improper conduct of the study by the investigator, inability to obtain the number of subjects required by the protocol, etc. Reimbursement for reasonable expenses will be made if such action is necessary.