TITLE PAGE

Protocol Number: C-17-EV11

Protocol Title: Open-label, Prospective, Multicenter Study to Evaluate the Cutera Excel V™ Laser and a Micro-Lens Array Attachment

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Version, Date: Version 2.0- Dated: September 12, 2017

Statement of Compliance
The study will be conducted in accordance with the design and specific provisions of this IRB approved protocol, in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and that are consistent with Good Clinical Practice (GCP) and the applicable regulatory requirement(s).

NOTE: The confidential information in the following document is provided to you as an Investigator, potential Investigator, or consultant for review by you, your staff, and applicable Institutional Review Board. By accepting this document, you agree that the information contained herein will not be disclosed to others, without written authorization from Cutera, Inc. except to the extent necessary to obtain informed consent from those persons to whom the device will be administered.

Protocol Signature Sheet – Principal Investigator

PROTOCOL C-17-EV11

Study Title: Open-label, Prospective, Study to Evaluate the Cutera Excel V™ Laser and a Micro-Lens Array Attachment

Protocol Version 2.0, Date: 12SEP2017

I have received and read the protocol dated September 12, 2017 and agree to adhere to the requirements. I am aware that my adherence to the above protocol is mandatory and that any changes in the protocol or informed consent form must first be approved by Cutera, Inc. and the Institutional Review Board, except those changes necessary to eliminate apparent immediate hazards to subjects. I will provide copies of this protocol and all pertinent information to the study personnel under my supervision. I will discuss this material with them and ensure they are fully informed regarding their role in the study. I will ensure that the study is conducted in compliance with the protocol, Good Clinical Practice (GCP), and all applicable regulatory requirements, and with the reviewing Institutional Review Board (IRB) requirements. I agree to commence this study only after documented IRB approval is obtained.

Principal Investigator

_____	_____
Signature	Date
_____	_____
Printed Name	Date

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Protocol Summary

Title	Open-label, Prospective, Study to Evaluate the Cutera Excel V Laser and a Micro-Lens Array Attachment
Objective	a. To evaluate the safety of the Cutera excel V laser and a Micro-Lens Array attachment. b. To evaluate the efficacy of the Cutera excel V laser and a Micro-Lens Array attachment.
Study Design	Open-label, Prospective, Study to Evaluate the Cutera excel V laser at 532 nm in a low fluence, high repetition rate mode and the Micro-Lens Array attachment used with excel V laser at 1064 nm and 532 nm for the improvement of skin quality.
Enrollment	Approximately 60 subjects will be treated
[redacted] **Endpoint**	• Safety of the Cutera excel V laser and the Micro-Lens Array attachment assessed by the frequency and severity of device related adverse events.
[redacted] **Endpoints**	• Efficacy of treatment(s) with Cutera excel V laser and the Micro-Lens Array attachment as assessed by the study investigator f[redacted] for the improvement of skin quality. • [redacted].
[redacted]	• [redacted]
Subject Population	Female or male subjects, age 18 to 65 years, Fitzpatrick skin types I-VI
Estimated Planned Schedule	First subject enrolled: September 2017 Last subject last visit: November 2018

1. BACKGROUND INFORMATION

Non-invasive treatment options are in high demand by patients wanting to improve their appearance without surgical intervention. As a result, patients now have a variety of options for non-invasive skin rejuvenation, from laser and light-based treatments to devices that utilize ultrasound and radiofrequency, however this was not always the case. Initial skin rejuvenation procedures utilized ablative lasers, such as the carbon dioxide (CO2) and erbium:yttrium-aluminum-garnet (Er:YAG), and resulted in substantial improvement in skin appearance, texture, rhytides and laxity[1-3]. However, since ablative treatments destroy the epidermal layer of the skin in order to penetrate and heat the deeper dermal layers, ample post-procedure recovery time is required and patients may experience side effects lasting for a few weeks. Furthermore, hypo- or hyperpigmentation, prolonged wound healing and even scarring can occur following ablative procedures [4-6]. Treatment methods with less risk of side effects and post-treatment down time are in high demand. As such, the choices are vast and varied, ranging from fractional non-ablative laser devices to those that use radiofrequency [7-15]. Fractional lasers inflict microscopic zones of thermal damage in the dermal layers of the skin without destruction of the epidermis, thereby reducing recovery time significantly as compared to ablative procedures[16]. Treatment with non-fractional, non-ablative laser devices requires little to no post-procedure recovery time. Nonablative lasers of various wavelengths are effective for skin rejuvenation based on the principle of selective photothermolysis, whereby laser light is absorbed by hemoglobin in blood vessels and melanin in pigment-producing skin cells [17, 18]. Absorption of laser light by these molecular chromophores results in the production of heat, leading to destruction of unwanted blood vessels and pigment cells. Heat production within the dermis by the laser light also results in immediate collagen contraction and heat-induced wound healing that, over time, causes a cascade of cellular events leading to new collagen production and improved skin appearance [8, 10, 19-23].

[redacted]

[redacted]

2. [redacted]

[redacted],

[redacted]

3. STUDY OBJECTIVES

The objectives of this pivotal study are:

a. To evaluate the safety of the Cutera excel V laser and the Micro-Lens Array attachment.

b. To evaluate the efficacy of the Cutera excel V laser and the Micro-Lens Array attachment in the improvement of skin quality.

4. STUDY DESIGN

This is an open-label, prospective, study in approximately 60 male or female subjects, age 18 to 65 years who desire laser treatment for the improvement of rhytides, lentigines, pigmentation, erythema, telangiectasia, pore size and skin texture. [redacted]. Subjects will receive [redacted] laser treatments, [redacted]. Subjects will be contacted by phone 7 days [redacted]) after their first treatment for follow-up. Subjects will return to the site after final study treatment for two follow-up visits: 6 and 12 weeks [redacted]).

4.1 Study Endpoints

4.1.1 [redacted] Safety Endpoint

Safety of the Cutera excel V laser and the Micro-Lens Array attachment assessed by the frequency and severity of device related adverse events.

4.1.2 [redacted] Efficacy Endpoints

- Efficacy of treatment(s) with Cutera excel V laser and the Micro-Lens Array attachment as assessed by the study investigator from the 2nd treatment onward for the improvement of skin quality.
- Subject satisfaction levels as assessed from the subject questionnaire.

4.1.3 [redacted]

[redacted].

4.2 Study Duration

Subjects enrolled in this trial will participate for approximately 14 months, [redacted], [redacted], and 2 follow-up visits at 6 and 12 weeks [redacted]) post final treatment. In

total, enrolled subjects will complete up to 9 visits: 1 screening visit, 1 week phone follow-up after first treatment, up to [redacted] laser treatment visits, and 2 required follow-up visits.

The screening and first laser treatment may be combined into one visit provided that the subject has signed the IRB-approved Informed Consent Form prior to the commencement of any study-related procedures and has met all criteria to be enrolled in the study.

4.3 Study Effectiveness Assessments

4.3.1 Investigator Assessments

At baseline, and starting after the second treatment, the Investigator will assess the efficacy of the Cutera excel V laser with the MLA attachment treatment using the GAIS, [redacted] Baseline photos of subjects may be used while assessing the GAIS, [redacted]

Global Aesthetic Improvement Scale (GAIS): [Only performed after treatment]
4 = Very Significant Improvement [redacted]
3 = Significant Improvement [redacted]
2 = Moderate Improvement [redacted]
1 = Mild Improvement [redacted]
0 = No Change [redacted]

[redacted]

[redacted]

4.4 Study Safety Assessments

4.4.1 Incidence and Severity of Adverse Events:

Following the first laser treatment, adverse effects (AEs) will be assessed post-treatment and at each subsequent visit using the following scale:

1= mild: requires minimal or no treatment and does not interfere with the subject’s daily activities.
2= moderate: may cause some interference with functioning.
3= severe: interrupts subject’s usual daily activity and may require treatment.

4.4.2 Treatment-related Discomfort

After each laser treatment, subjects will be asked to rate the average amount of discomfort experienced during treatment and immediately after laser treatment.

4.4.3 [redacted]

[redacted]

4.5 Photographs

Standardized digital photographs will be taken of each subject's treatment area at baseline, prior to and post all laser treatments and at each follow-up visit. Treatment area will be cleansed and any jewelry and make-up will be removed from the area being photographed. For facial photographs, hair will be pulled away from the face with a headband.

Facial photographs will be obtained from at least 3 angles: with the subject facing forward, 45° to the right and 45° to the left. Photographs will be taken in the same windowless room equipped with adequate lighting. The room lighting, camera positioning and subject positioning should be consistent for all study visit photographs. Digital camera settings should remain the same for all photographs and the highest resolution settings should be utilized.

4.6 Study Discontinuation

Cutera, Inc. (the sponsor) has the right to terminate this study at any time. Reasons for terminating the study may include, but are not limited to, the following: incidence or severity of adverse events in this or other studies indicates a potential health hazard to subjects; subject enrollment is unsatisfactory; number of protocol deviations is unacceptable; data recording is inaccurate or incomplete; or questionable study site compliance with ICH-E6, Good Clinical Practice[23].

4.7 Investigator Selection

The Investigator(s) will be invited to participate in the study based on his or her medical specialty, experience conducting clinical research studies and experience in the use of light-based devices for aesthetic indications. Access to potential study subjects and the Investigator's sincere interest in this study along with expressed willingness to cooperate with the study process and requirements was also considered.

5. STUDY POPULATION

5.1 Study Subject Recruitment and Selection

Approximately 60 male or female subjects, ages 18 to 65, with Fitzpatrick Skin Type I-VI who desire laser treatment for rhytides, lentigines, pigmentation, pore size, acne scars, erythema, telangiectasia and skin texture. Subjects will be recruited to participate from the local population. Subjects may also be recruited from the Investigator's existing patient database or from patients who present themselves to the study site requesting treatment. Only subjects who meet all eligibility criteria and who provide written informed consent will be enrolled into the study.

Each subject will be evaluated by the Investigator to assess his/her suitability for entry into the study according to the following inclusion and exclusion criteria.

5.1.1 Inclusion Criteria

To be included in the study, subjects must meet all of the following Inclusion Criteria:

1.	Subject must be able to read, understand and sign the Informed Consent Form.
2.	Female or Male, 18 to 65 years of age (inclusive).
3.	Fitzpatrick Skin Type I – VI.
4.	Must be willing to have Cutera excel V laser treatments and able to adhere to the treatments, follow-up visit schedule, and post-treatment care instructions.
5.	Willing to have very limited sun exposure and use sunscreen on the treatment area every day for the duration of the study, including the follow-up period.
6.	Willing to have digital photographs taken of the treatment area and agree to use of photographs for presentation (educational and/or marketing), publications, and any additional marketing purposes.
7.	Agree to not undergo any other cosmetic procedure(s) or treatment(s) on the face during the study and has no intention of having such procedures performed during the course of the study.
8.	For female subjects: not pregnant or lactating and is either post-menopausal, surgically sterilized, or using a medically acceptable form of birth control at least 3 months prior to enrollment and during the entire course of the study.,

5.1.2 Exclusion Criteria

Subjects will be excluded from the study if they meet any of the following Exclusion Criteria:

1.	Participation in a clinical trial of another drug, or device administered to the treatment area, within 3 months prior to enrollment or during the study.
2.	Any type of prior cosmetic treatment to the target area within 6 months of study participation, such as laser procedures, facial fillers, toxins and those used for general aesthetic correction.
3.	Use of prescription topicals in the treatment area within one month prior to treatment or use of topical agents one week prior to treatment that may cause facial sensitivity.
4.	Suffering from significant skin conditions in the treated areas or inflammatory skin conditions, including but not limited to, open lacerations or abrasions, hidradenitis, rash, infection , or dermatitis of the treatment area prior to treatment (duration of resolution as per the Investigator's discretion).
5.	Pregnant and/or breastfeeding, or planning to become pregnant.
6.	Significant concurrent illness, such as diabetes mellitus, immunosuppression/immune deficiency disorders (including HIV infection or AIDS) or using immunosuppressive medication.
7.	Hypersensitivity to light exposure.
8.	Any use of medication that is known to increase sensitivity to light according to the Investigator's discretion.

9.	History of keloid scarring, hypertrophic scarring or abnormal wound healing or prone to bruising.
10.	Has a history of squamous cell carcinoma or melanoma in the treatment area.
11.	History of epidermal or dermal disorders (particularly if involving collagen or microvascularity), including collagen vascular disease or vasculitic disorders.
12.	A history or active skin condition that in the opinion of the Investigator may interfere/confound with the treatment.
13.	History of connective tissue disease, such as systemic lupus erythematosus or scleroderma.
14.	History of disease stimulated by heat, such as recurrent herpes simplex and/or herpes zoster (shingles) in the treatment area, unless treatment is conducted following a prophylactic regimen.
15.	History of pigmentary disorders, particularly tendency for hyper- or hypo-pigmentation, or any that are considered not acceptable by the study investigator.
16.	Has used oral isotretinoin (Accutane or therapeutic vitamin A supplements of ≥ 10,000 units per day) within 12 months of initial treatment or plans on using during the course of the study (note: skin must regain its normal degree of moisture prior to treatment, e.g. lack of noticeable skin flaking and peeling).
17.	Excessively tanned or active sun tan in facial area to be treated, or unable/unlikely to refrain from tanning during the study.
19.	Excessive facial hair in the area to be treated (beards, sideburns, and/or moustache,) that would interfere with diagnosis, assessment, and treatment.
20.	As per the Investigator's discretion, any physical or mental condition which might make it unsafe for the subject to participate in this study, including excessive alcohol or drug abuses, or a condition that would compromise the subject's ability to comply with the study requirements.

5.2 Subject Numbering

If a subject completes the Informed Consent Form, meets the study eligibility criteria and is willing to participate, the subject will be assigned a study subject identification number. This number is comprised of a site number (which is provided by the sponsor) and a sequential subject number and the subject initials (first and last names).

5.3 Subject Discontinuation Criteria

If possible, every subject should remain in the study until completion of the required follow-up period. However, participation in this study is completely voluntary and a subject can choose to withdraw from the study at any time. Decision to withdraw will not affect or prejudice the subject's continued medical care in any way. In those instances, the investigator will attempt to obtain a final clinical assessment and an adverse device effect evaluation for the subject prior to this withdrawal. A subject will be considered lost to follow-up only after three unsuccessful, documented attempts to contact the subject have been made.

In addition, a subject can be discontinued for any of the following reasons: the Principal Investigator decides that continuing in the study would not be in the subject's best interest, a subject is noncompliant

with the protocol, a subject has a serious reaction to the treatment, a subject develops any of the exclusion criteria during the study period or the study is stopped by the study sponsor.

6. STUDY PROCEDURES

A summary of all study required procedures and assessments can be found in Appendix 1.

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[redacted]	[redacted]	
[redacted]	[redacted]	

[redacted]

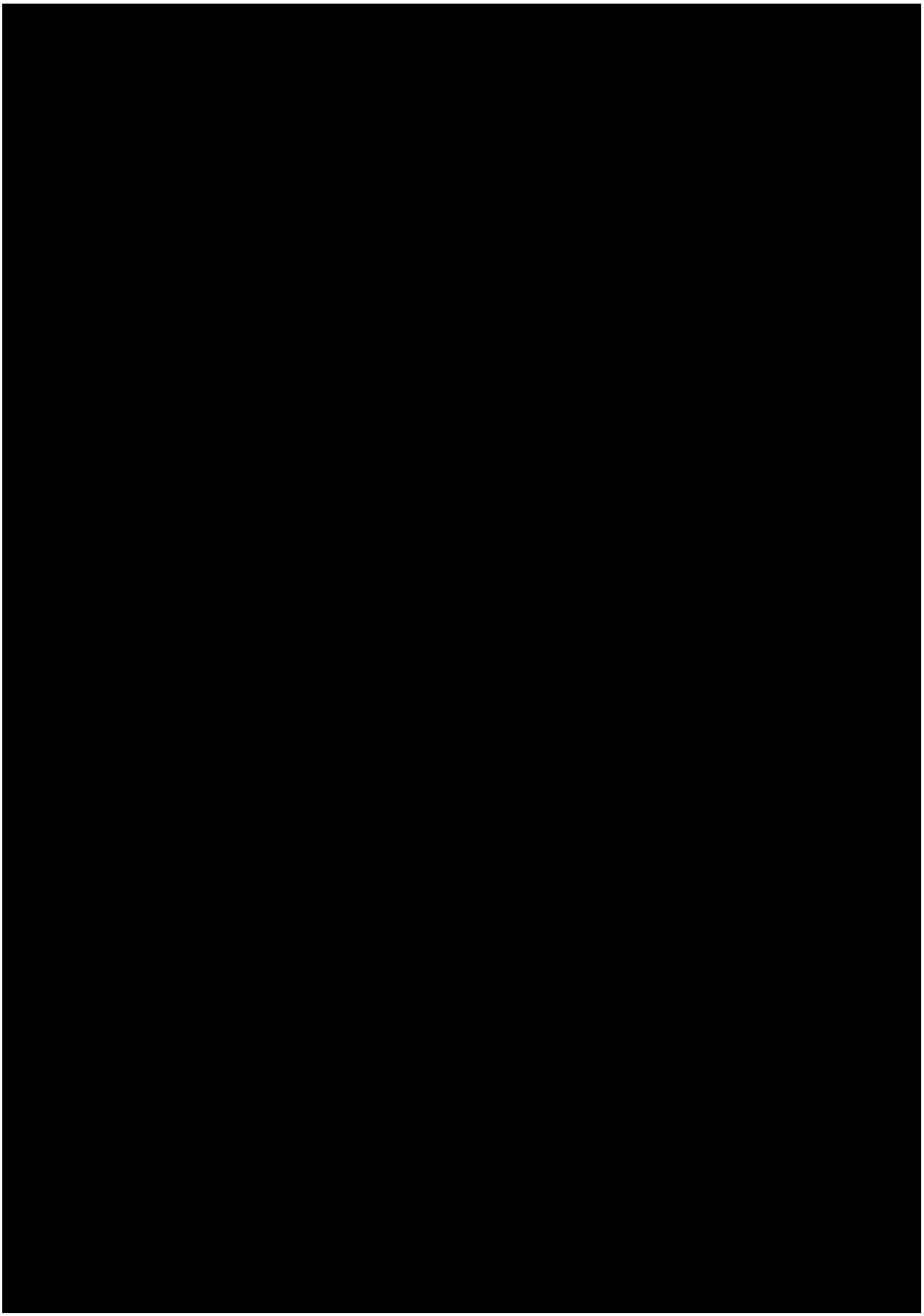
[redacted].

[redacted]

7. ADVERSE EVENTS and ADVERSE DEVICE EFFECTS

7.1 Definitions

[redacted]



7.2 Recording AEs, EADEs, ADEs and SADEs

All AEs/SAEs or EADEs/ADEs/SADEs will be: (1) evaluated and must be recorded in the subject's medical chart and in the study case report forms (CRFs); (2) monitored and tracked from the time of the first treatment with the Cutera Excel V laser system.

At each contact with the subject, the investigator must seek information on AEs/EADEs/ADEs/SADEs by specific questioning and, as appropriate, by examination. AEs/ADEs/SADEs may be observed by the investigator and/or clinical research staff, elicited from the subject and/or family member or volunteered by the subject. All observed and volunteered adverse signs and symptoms, anticipated or unanticipated, regardless of severity or frequency, will be recorded in the case histories (medical chart and CRFs). Included in the description should be the nature of the sign or symptom, the date of onset, date of resolution (duration), the severity, anticipated or unanticipated, the relationship to study treatment or other therapy, the action taken (if any), and the outcome.

All SAEs/SADEs, anticipated or unanticipated, must be reported to Cutera immediately but not later than 5 working days. The SADE must be recorded in: (1) the AE CRF and (2) a written report must be submitted to Cutera within five (5) working days after the investigator first learns of the event and is to include a full description of the event and sequelae, in the format detailed by the Cutera Serious Adverse Event Form.

7.3 Follow-up of subjects after AEs/ADEs and SAEs/SADEs:

All reported AEs/ADEs/SAEs/SADEs should be followed until resolution or until the subject's participation in the study ends. Resolutions of AEs/ADEs/SAEs/SADEs are to be documented on the appropriate CRFs. All ADEs that result in permanent discontinuation from this clinical trial, whether serious or not, should also be reported on the subject Non-Completion of Study Form.

8. POTENTIAL RISKS / BENIFITS

[redacted]

[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
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[redacted]

[redacted]

8.2 Potential Benefits

The subjects may or may not benefit from the treatment with the study device. Potential benefit of laser treatment is improved in the appearance of the skin. There is no guarantee of success.

9. RISK MANAGEMENT

The investigator participating in this study was chosen based on extensive and safe experience with the use of lasers in dermatology applications. This is the most critical element in managing subject risk. In addition, study investigators will be trained on the use of the Cutera excel V laser system by a representative of Cutera.

10. DATA ANALYSIS PLAN

10.1 Sample Size

The planned sample size of approximately 60 subjects has been deemed sufficient for the evaluation of the excel V with an MLA attachment.

10.2 Statistical Analysis Methods

This is a study to evaluate safety and efficacy of the Cutera excel V laser with the Micro-Lens Array attachment. Outcome measures will be assessed around multiple endpoints. These measures will be: degree of improvement as assessed by the Investigator, [redacted] and safety. Formal hypothesis testing and statistical analysis are not planned for this study.

10.3 Safety Analyses

Safety variables will be analyzed descriptively. The safety variables for this study are:

- Incidence and severity of adverse effects during study duration (to be displayed descriptively as counts and frequency distributions)

Enrolled subjects who received at least one treatment will be included in the safety analyses. Device-related and procedure-related adverse effects (AEs) and subjects who prematurely terminate from the study due to an adverse device effect, including the treatment-related pain/21iscomfort ratings, as reported on case report forms will be tabulated and analyzed. For a given AE term, counting will be done by subject, not by event, i.e. for a subject reporting the same AE more than once, the event will be counted only once, at the most severe and most-related occurrence. The number and percentage of subjects experiencing each AE Term will be descriptively summarized. Statistical hypothesis testing will not be performed for safety data.

12. [redacted]

[redacted]

[redacted]

12.3 Protocol Compliance

The principal investigator must comply with all terms of the protocol.

12.4 Protocol Amendments

Neither the principal investigator nor the sponsor will modify or alter this protocol without first obtaining the concurrence of the other party (with the exception of amendments which involves mitigating a medical emergency or immediate health risk to the subject). The party initiating an amendment must confirm it clearly in writing and it must be signed and dated by the sponsor and the principal investigator. IRB approval must be obtained before implementation of an amendment.

12.5 Protocol Deviations

All protocol deviations must be clearly described on the case report form (i.e., Cutera Protocol Deviation Form). Deviations from the protocol may include but are not limited to subject's failure to attend scheduled visit during a visit window, use of out of range treatment parameters and incomplete or incorrect study procedures. Any medical emergency or immediate health risk to the subject which results in a protocol deviation and must be reported to the sponsor within 5 working days.

Significant protocol deviations must be reported to IRB according to their policies.

12.6 Study Personnel

The investigator must supply the sponsor with a list of the names and curricula vitae that describe the professional backgrounds of the clinically responsible study investigators (principal, sub-investigators), research nurses, and other possible participants (e.g. medical doctor, nurse, etc.).

12.7 Disclosure of Financial Interest

Each investigator [principal and sub-investigator(s)] is required to disclose sufficient accurate financial information to the sponsor, to allow sponsor to submit complete and accurate certification or disclosure statements.

12.8 [redacted]

[redacted]

13. SUBJECT CONFIDENTIALITY

This study preserves the confidentiality of all subjects under the Health Insurance Portability and Accountability Act of 1996 (HIPAA) Privacy Rule. The following safeguards will be in place to protect the privacy of the individuals who are the subjects of the health information to be used in the research and the confidentiality of that information:

[redacted]

[redacted]

14. PUBLICATION POLICY

The investigator shall have the right to publish the results of the study. Unless mutually agreed upon in writing, prior to submission for publication of any manuscript, poster, presentation, abstract or other written or oral material describing the results of the study, the investigator shall allow sponsor to review manuscript, poster presentation, abstract or other written or oral material which describes the results of the study for the purpose only of determining if any patentable information is disclosed. At the sponsor's request, the investigator shall withhold any publication or presentation to permit sponsor to seek patent protection and to remove any confidential information from all publications.

The International Committee of Medical Journal Editors (ICMJE) member journals have adopted a trials registration policy as a condition for publication. This policy requires that all clinical trials be registered in a public trials registry such as ClinicalTrials.gov, which is sponsored by the National Library of Medicine. It is the responsibility of the sponsor to register this trial in ClinicalTrials.gov. Any clinical trial starting enrollment after September 27, 2007 must be registered either on or before the onset of patient enrollment.

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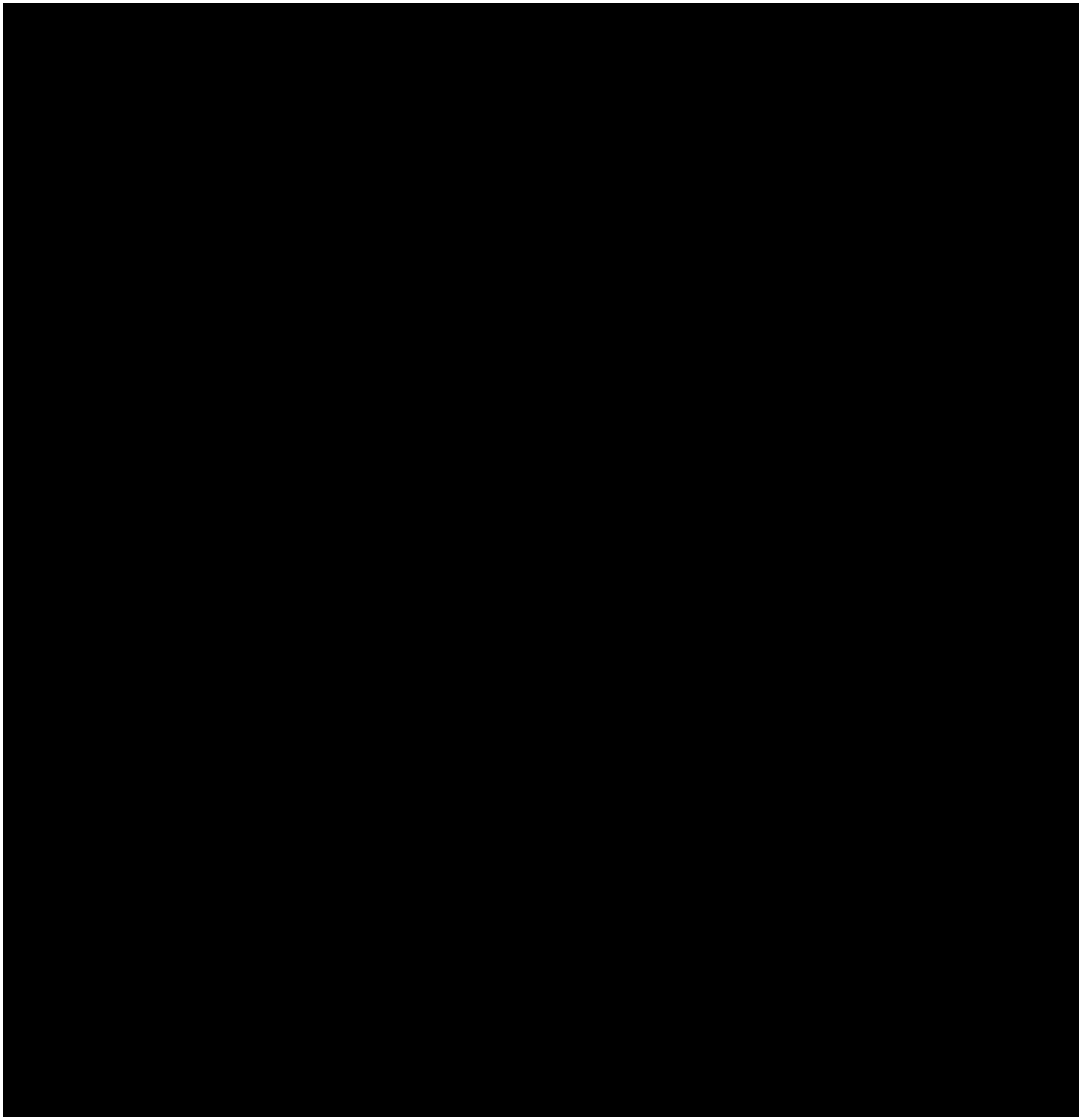

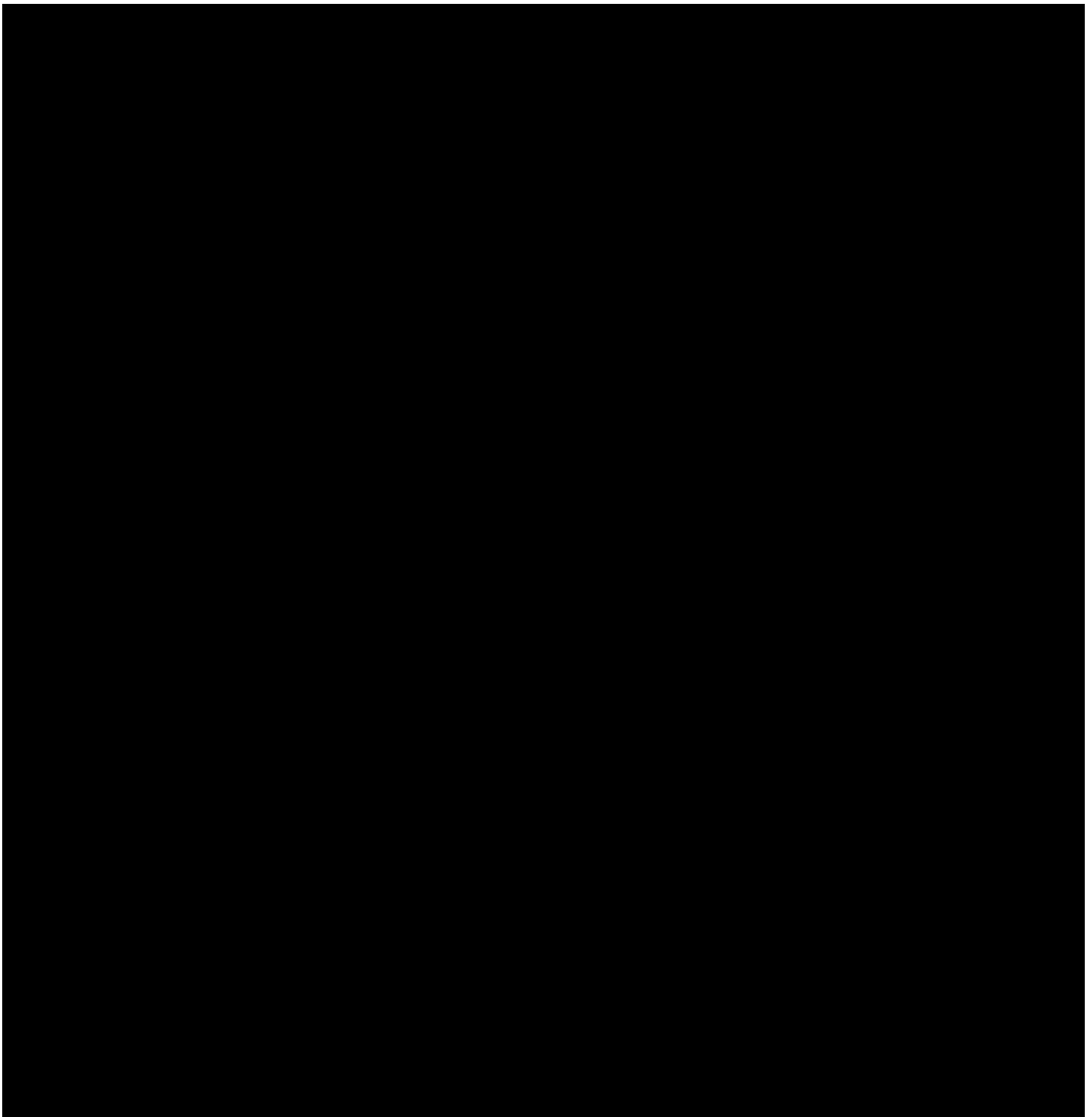

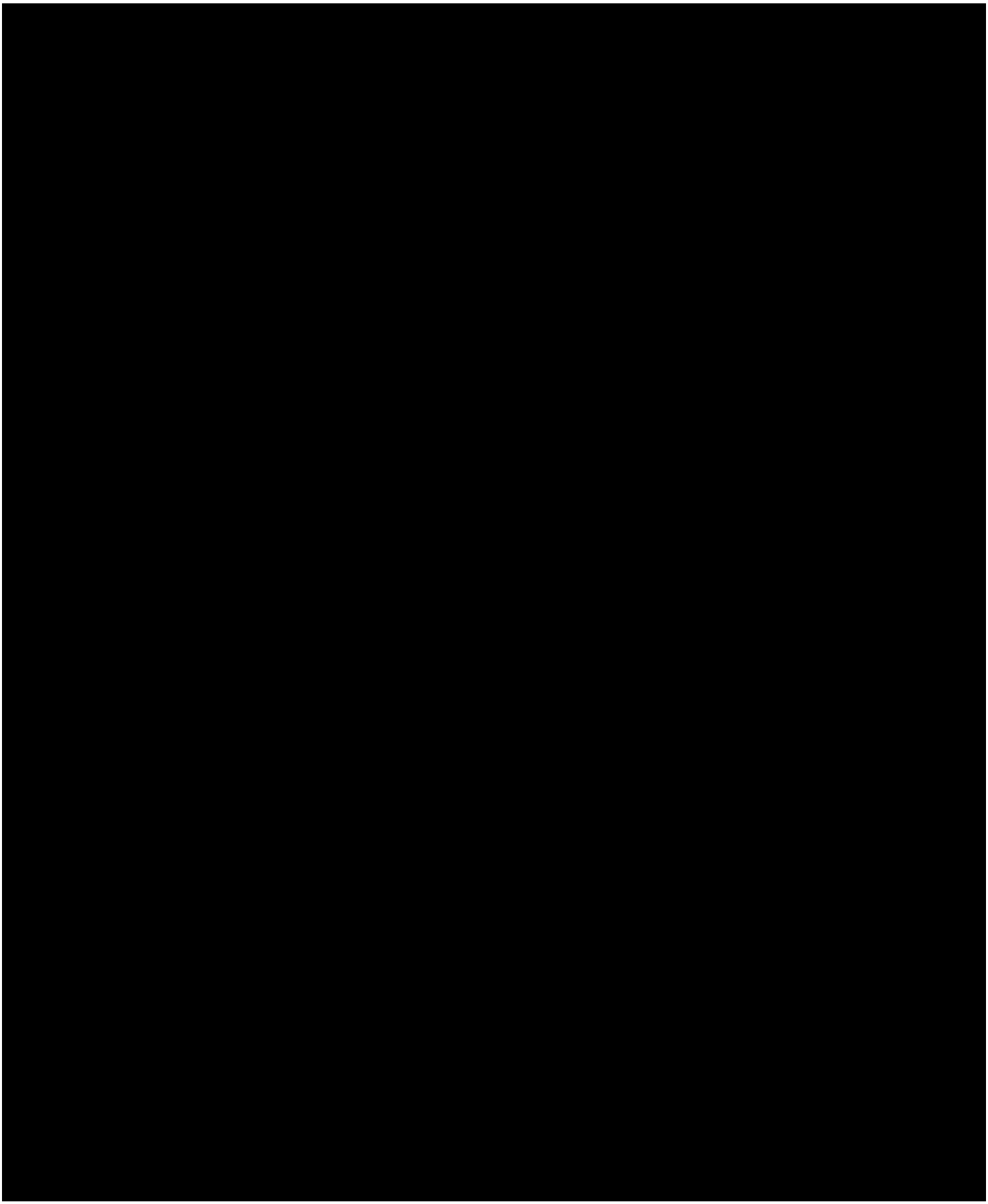

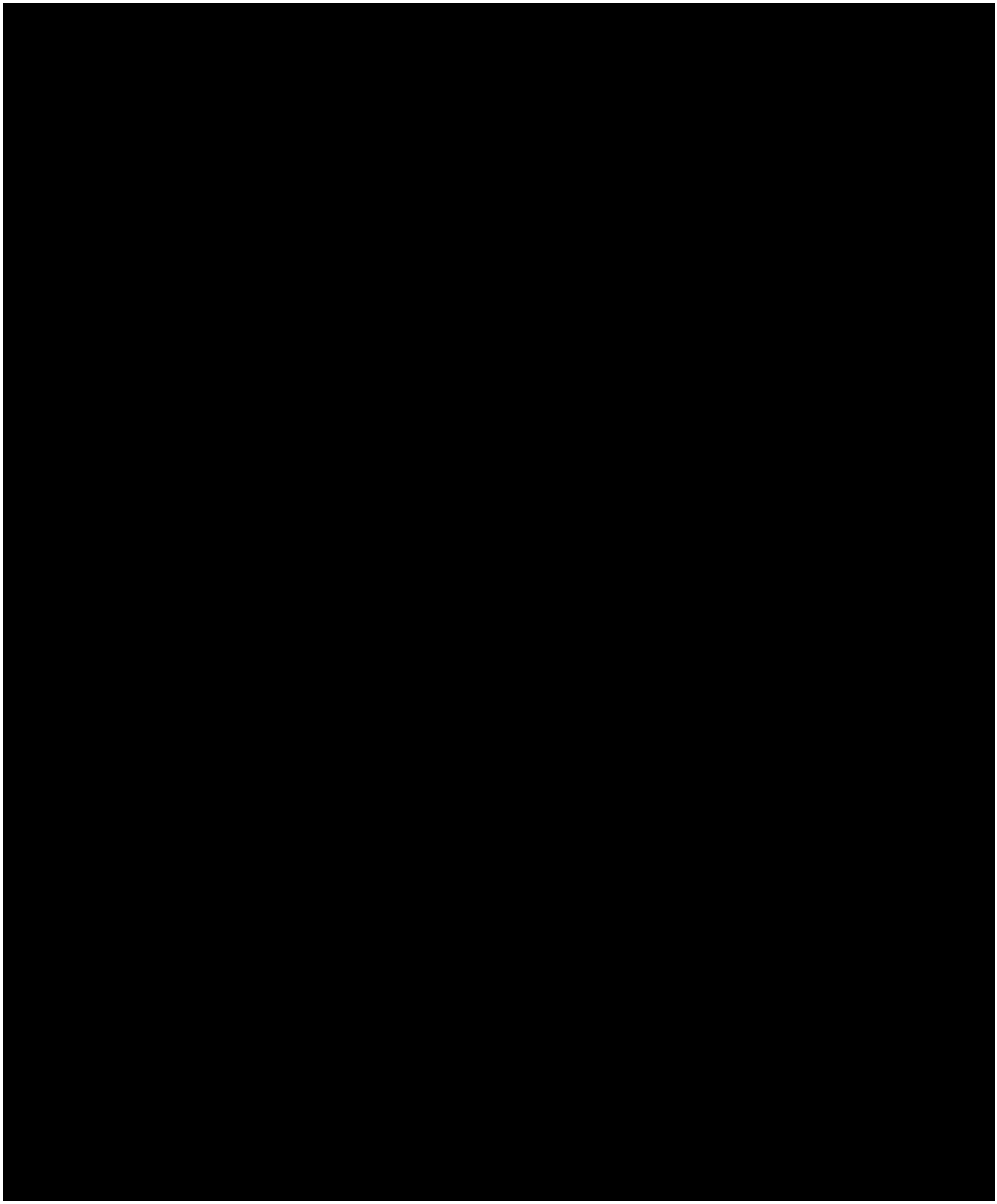

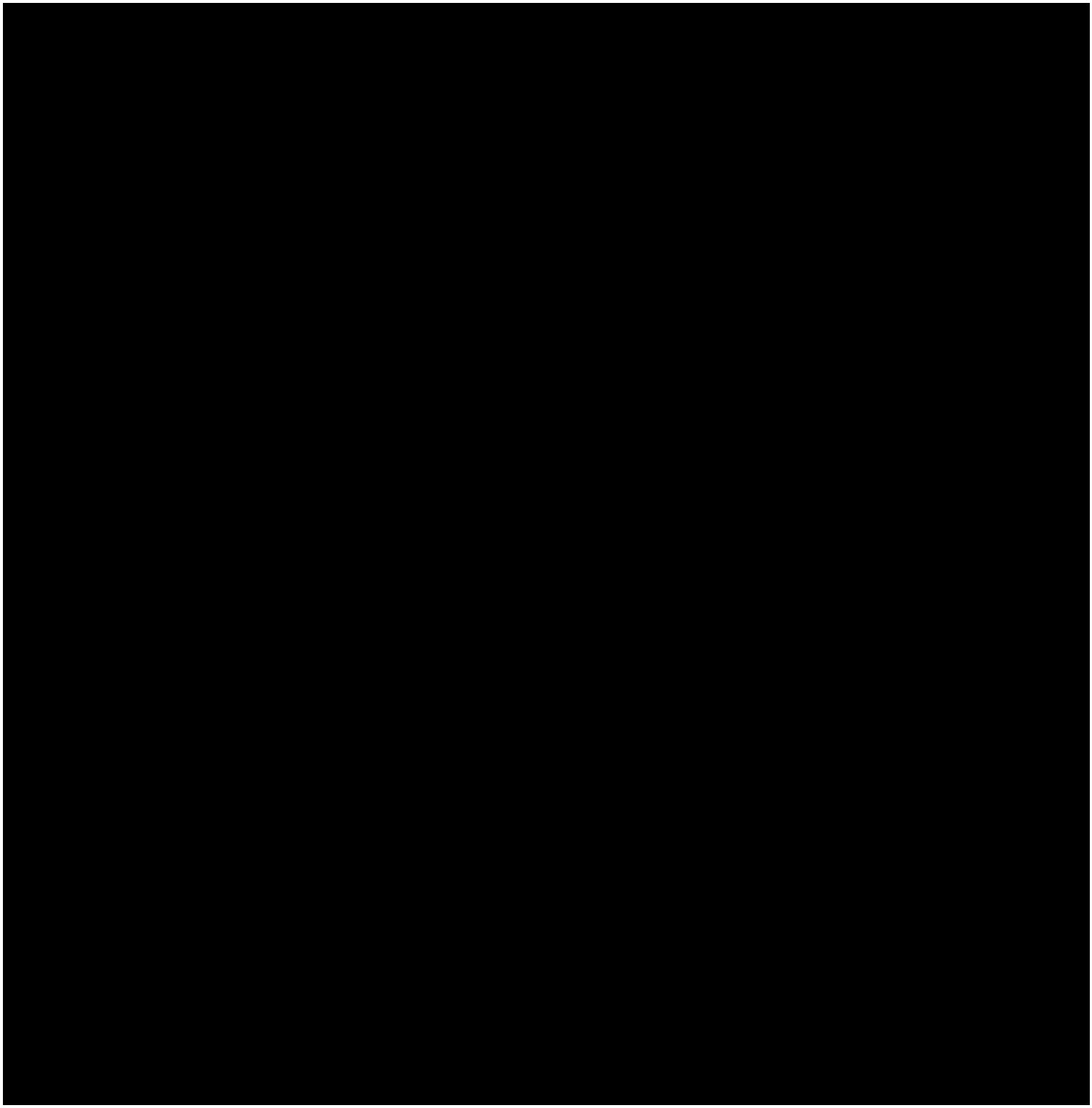

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