TITLE PAGE

Protocol Number: C-20-PAC01

Protocol Title: A Safety and Efficacy Study of a 1726nm Laser for the Treatment of Acne Vulgaris

Sponsor: Cutera, Inc.
3240 Bayshore Boulevard
Brisbane, CA 94005

[redacted] Dated April 16, 2021

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, applicable Institutional Review Board (IRB), and US Food and Drug Administration (FDA). 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/assent from those persons to whom the device will be administered.

Protocol Signature Page – Principal Investigator

PROTOCOL C-20-PAC01

Study Title: ***A Safety and Efficacy Study of a 1726nm Laser for the Treatment of Acne Vulgaris***

[redacted]

I have received and read the protocol dated **April 16, 2021** 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/assent form must first be approved by Cutera, Inc., the Institutional Review Board (IRB), and the US Food and Drug Administration (FDA) according to their policies except those changes necessary to eliminate apparent immediate hazards to subjects. I will ensure copies of this protocol and all pertinent information are provided to the study personnel under my supervision. I will ensure this material is discussed with them and they are fully informed regarding their role in the study. I will ensure that the study is conducted in compliance with the protocol, IRB guidelines, Good Clinical Practice (GCP), FDA 21 CFR part 812 and all other applicable regulatory requirements. I agree to commence this study only after documented IRB and FDA approval is obtained.

Principal Investigator

_____ _____

Signature Date

_____

Printed Name

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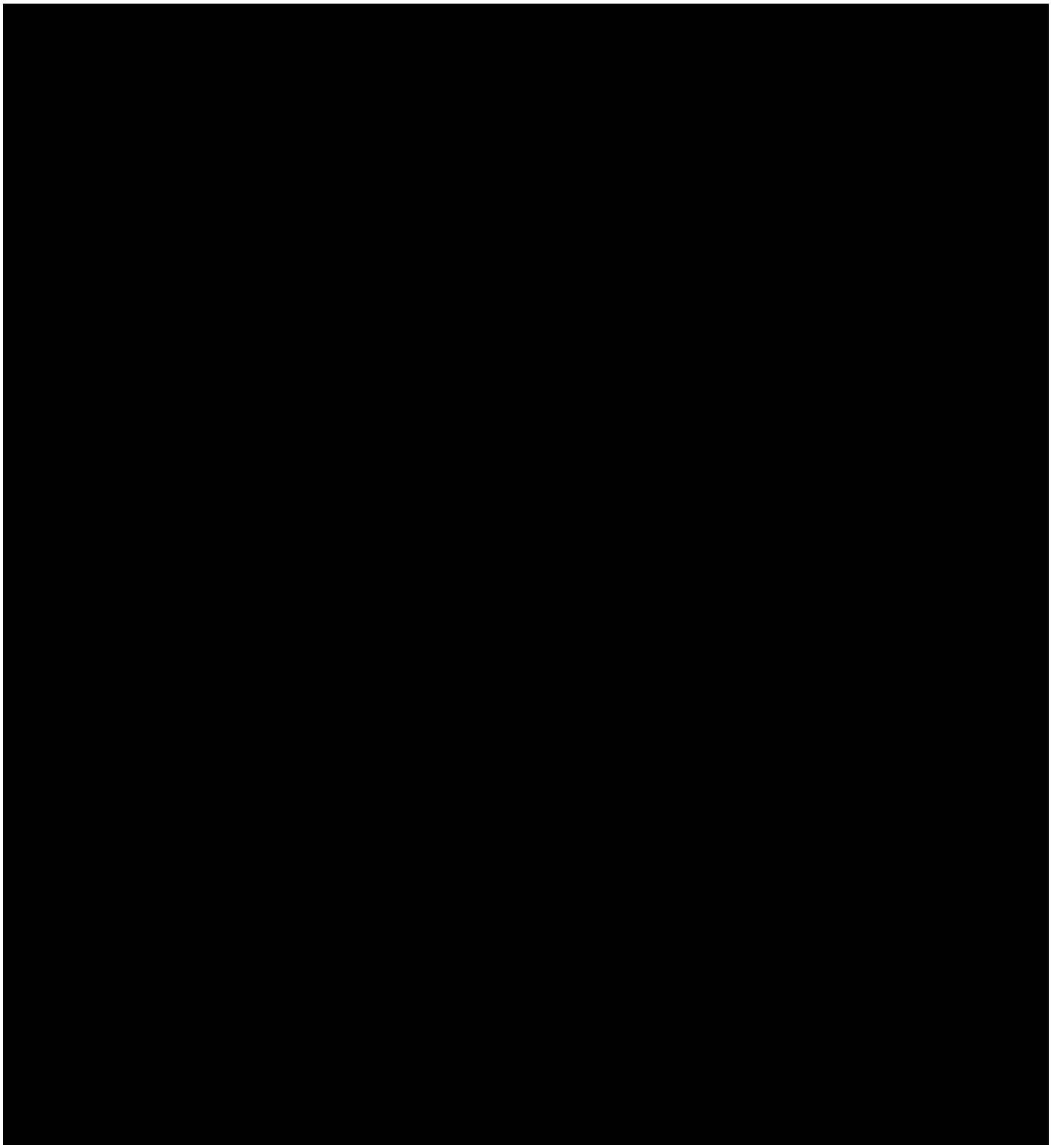
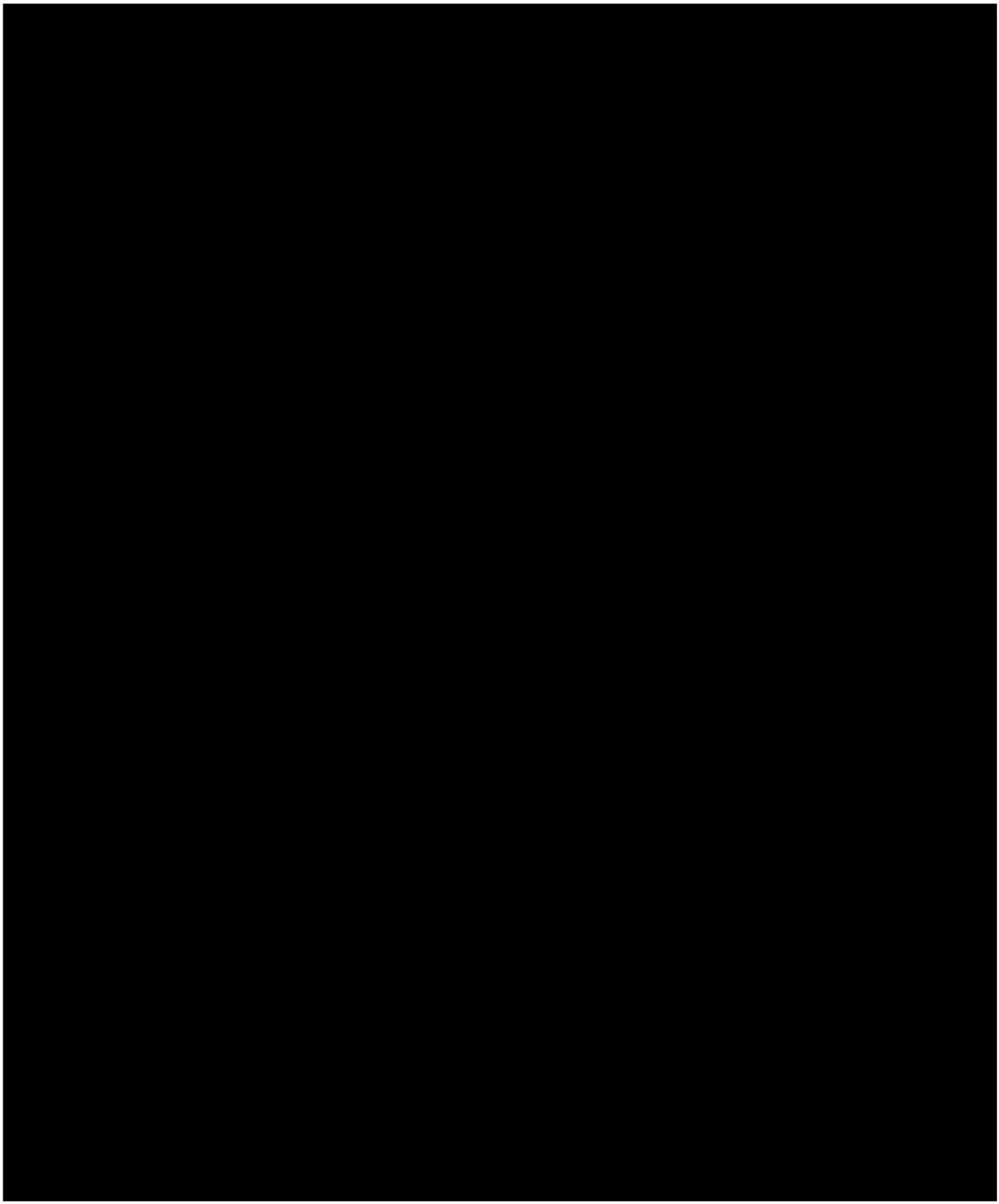




1 PURPOSE

The purpose of this pivotal investigation is to evaluate the safety and efficacy of the investigational Cutera® 1726 nm laser system ([redacted] for the treatment of mild to severe acne vulgaris. Data from this investigation is intended to support a future 510(k) submission to obtain marketing clearance for the intended use listed above.

2 BACKGROUND INFORMATION

2.1 Acne Vulgaris

Acne Vulgaris is one of the most common dermatological conditions and affects a significant number of adolescents and adults.[1, 2, 3] It develops in the pilosebaceous units of the skin from the following four factors—excess sebum production, the presence of the *Propionibacterium acnes* (*P. acnes*) bacteria, follicular epidermal hyper proliferation that plugs the follicle, and inflammation. It can have severe psychological effects and can leave the patient with severe skin scarring.[3, 4, 5, 6]

Currently, standard acne treatment includes the use of topical and systemic medications, with the choice of treatment often determined by disease severity, but also by patient preferences and cost considerations.[5]

Topical treatments work to reduce the level of follicle obstruction and reduce the bacterial load and inflammation. Of the topical medications, retinoids, benzoyl peroxide, azelaic acid, salicylic acid, and antibiotic solutions are used regularly, either alone or in combination with other treatments. Combinations have been reported to increase effectiveness, especially with benzoyl peroxide or retinoids and topical antibiotics such as clindamycin, erythromycin, or tetracycline. Topical retinoids are indicated as a first-line treatment in patients with non-inflammatory lesions.[6] Because the use of topical antibiotics may lead to resistance in the *P. acnes* bacteria, the use of benzoyl peroxide, retinoids, and other non-antibiotic medications are an important adjunct to antibiotic therapy. [3, 6]

Systemic medications include oral antibiotics, anti-androgens, and isotretinoin. Oral antibiotics, among other potential mechanisms of action, target bacteria and directly reduce inflammation. Oral anti-androgens such as low estrogen oral contraceptives, are indicated after failure of standard antibiotic regimens, and act to reduce the sebum driving effects of testosterone. [5] Oral isotretinoin has remained the most effective systemic medication for moderate to severe acne as well as for refractory cases. It acts to affect cell progression, differentiation, survival, and apoptosis, as well as reduces sebum production, comedogenesis, *P. acnes* load, and inflammation.[5, 6, 7]

Each of these treatments has its limitations. For example, oral isotretinoin has serious side effects of teratogenicity and possibly psychiatric effects, which can limit the safety and utility of the drug for many patients.[7] Although topical and oral antibiotics have been used successfully in the treatment of acne for decades, the concern over antibiotic resistance continues to grow.[3] As such, alternative, yet effective new treatments are still needed. While topical and systemic medications remain the gold standard for treatment of acne vulgaris, laser therapy which has emerged in recent decades as an effective treatment of acne vulgaris may be an additional option for some patients, especially for those who cannot tolerate standard treatments or for refractory cases.[6]

There are two main mechanisms of action for treatment of acne with light therapy. First, blue or red light sources, green or yellow light lasers, and intense pulsed light (IPL) devices kill *P. acnes* directly. Second,

radiofrequency (RF) devices and near infrared light lasers damage sebaceous glands.[6] Blue and red LED light sources have resulted in variable, but successful treatment of inflammatory acne.[8, 9] Mid-infrared devices, in the ranges of 1320 and 1450 nm lasers (which mainly target water and to a much lesser extent sebum), have shown efficacy in treating acne, but also may result in pain for the patient, which is a limitation to some of these treatments.[10, 11, 12] Photodynamic therapy (PDT) using red light at higher doses and longer incubation periods (≥ 3 hours) can directly inhibit sebaceous gland function through destroying sebocytes, but it is also associated with undesirable side effects such as intense pain during irradiation, long-lasting erythema, and oozing and crusting from epidermal damage.[6, 13, 14, 15]

Although the wavelengths above improve acne, none are preferentially absorbed directly by the sebaceous glands.[16] Exogenous chromophores introduced into the sebaceous gland complex (such as topically delivered light absorbing gold microparticles) help aid in sebaceous gland selective photothermolysis with infrared light, and the treatment is well-tolerated.[15, 16] Microparticles are currently indicated for use as an accessory to 1064 nm lasers to facilitate this photothermal heating of sebaceous glands for the treatment of mild to moderate inflammatory acne vulgaris [K181518].

[redacted]

[redacted]

[redacted]

[redacted]

3 STUDY OBJECTIVE

The primary objective is to evaluate the safety and efficacy of the investigational Cutera® 1726 nm laser system [redacted] for the treatment of mild to severe acne vulgaris. Data from this investigation is intended to support a future 510(k) submission to obtain marketing clearance for the intended use listed above.

4 STUDY DESIGN

This is a multi-center, prospective, open-label, single-arm study. Up to 15 study sites will enroll and initiate treatment on up to 107 male and female subjects, ages 16 to 60 years, who present with mild, moderate or severe facial acne at baseline, pass all eligibility criteria and desire laser treatment for their acne. Enrolled subjects will receive [redacted] laser treatments on the face [redacted]. Subjects will be followed at approximately 10 [redacted] days post each treatment (via phone) and at 4 [redacted], 12 [redacted] and 52 [redacted] weeks post-final treatment.

Subjects will be required to undergo a 1 month (30 day) washout period from topical retinoids and other systemic or topical acne medications prior to baseline, and for the duration of the study. If the acne medication is topical, the washout applies to use on the face only. [redacted]

4.1 Study Duration

Subjects enrolled in this study will be asked to participate for up to approximately 18 months [redacted]

4.2 Study Outcome Measures - Effectiveness

4.2.1 Primary Endpoint

The primary outcome measure to evaluate the efficacy of the investigational Cutera® 1726 nm laser system for the treatment of mild to severe acne vulgaris is the percent reduction in inflammatory acne lesion count across the entire face (excluding areas not treated) for each subject from baseline to 12 weeks [redacted]

[redacted]

4.3 Study Outcome Measures - Safety

Overall safety of the Cutera® 1726 nm laser system for the treatment of mild to severe acne vulgaris will be assessed by a review of the totality of all reported adverse events.

[redacted]

[redacted]

4.5 Safety Assessments

4.5.1 Incidence and Severity of Adverse Events

Following the first treatment, adverse events (AEs)/ adverse device effects (ADEs) will be assessed post-treatment and at each subsequent subject visit [redacted]

[redacted]

4.6 Photographs

Standardized digital photographs will be taken of each subject's face at baseline, prior to all laser treatments and at each follow-up visit, according to the following procedures:

- Subject will have recently cleansed skin;
- Subject's hair will be pulled away from his or her face;
- Subject will remove jewelry;
- A black drape will be placed around the subject's shoulders;
- A neutral facial posture will be maintained;

[redacted]

4.7 Study Discontinuation

The Investigator and/or 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 Good Clinical Practice, FDA 21 CFR Part 812 and other applicable regulations.

4.8 Investigator Selection

The Investigator(s) will be invited to participate in the study based on medical specialty, experience diagnosing and treating acne vulgaris, experience conducting clinical research studies and/or experience in the use of laser based devices for aesthetic indications and/or dermatology applications. 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 will also be considered.

5 STUDY POPULATION

5.1 Subject Recruitment and Selection

Male or female subjects, ages 16 to 60, with Fitzpatrick Skin Type I-VI[19] who present with mild, moderate, or severe facial acne vulgaris at baseline (and desire laser treatment for facial acne) will be included. Subjects will be recruited to participate from the local population. Subjects may also be recruited from the Investigator's or study site'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/assent will be enrolled into the study. [redacted]

Each subject will be evaluated 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.	Female or Male, 16 to 60 years of age (inclusive).
2.	[redacted] Fitzpatrick Skin Type I-IV[19]; [redacted] Fitzpatrick Skin Type V-VI[19]
3.	Has clinically diagnosed acne vulgaris of severity grade 2 – 4 on the face [redacted] using the Investigator's Global Assessment Scale [redacted]
4.	Has [redacted] inflammatory acne lesions on the face as determined by the Investigator (or qualified designee).
5.	Subject (and parent or legal guardian if subject is a minor under age 18) must be able to read, speak, and understand English and sign the Informed Consent Form.
6.	Willing to stop using topical retinoids and other acne medications for 1 month (30 days) prior to baseline and for the duration of the study. If the acne medication is topical, the washout applies to use on the face only.
7.	Willing and able to adhere to the treatment and follow-up schedule and pre/post-treatment care instructions.
8.	Willing to have very limited sun exposure (including avoiding tanning booths, sun lamps, sunbathing) and use an approved sunscreen of SPF 30 or higher on the face every day for the duration of the study, including the follow-up period.
9.	Willing to have photographs taken of the face and agree to the use of photographs for presentation, educational or marketing purposes.
10.	Agree to not undergo any other procedure(s) or add any new treatment modalities in the target area during the study.

5.1.2 Exclusion Criteria

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

1.	Has clinically diagnosed acne vulgaris of severity grade 0 or 1 on the face [redacted] using the Investigator's Global Assessment Scale.
2.	Prior treatment to the target area during participation in a clinical trial of another device or drug within 1 month (30 days) prior to study participation.
3.	Prior treatment to the target area within 3 months of study participation including chemical peel, dermabrasion, microneedling, radiofrequency treatment, laser or light-based procedures, cryodestruction or chemodestruction, intralesional steroids, photodynamic therapy, or acne surgery.
4.	Prior injection of botulinum toxin in the target area within 3 months of study participation and for the duration of the study.
5.	Prior injection of collagen, hyaluronic acid filler or other dermal filler in the target area within 6 weeks of study participation.
6.	Systemic use of retinoid, such as isotretinoin, within 6 months of study participation.
7.	History of malignant tumors in the target area.
8.	Excessive facial hair (e.g. beards, sideburns, moustaches, etc.) that would interfere with diagnosis or assessment of acne vulgaris in the target area (okay if shaved).
9.	Pregnant and/or breastfeeding or planning to become pregnant during the study.
10.	Presence of any skin condition in the target area (e.g. eczema, psoriasis, dermatitis, rash, papulo-pustular rosacea, infection) that would interfere with the diagnosis or assessment of acne vulgaris.
11.	Any medical condition that, in the opinion of the Investigator, would interfere with patient's participation in the full study protocol (e.g. severe Diabetes Mellitus or Cardiovascular Disease).
12.	Suffering from diagnosed coagulation disorders or taking prescription anticoagulation medications.
13.	History of diagnosed immunosuppression/immune deficiency disorders or currently using immunosuppressive medications.
14.	History of diagnosed connective tissue disease, such as systemic lupus erythematosus or scleroderma.
15.	Any use of medication that is known to increase sensitivity to light according to Investigator's discretion.
16.	History of disease stimulated by heat, such as recurrent herpes simplex and/or herpes zoster (shingles) in the target area, unless treatment is conducted following a prophylactic regimen.
17.	History of radiation to the target area, currently undergoing treatment for skin cancer in the target area, or undergoing systemic chemotherapy for the treatment of cancer.
18.	History of diagnosed pigmentary disorders (including vitiligo) in the target area.

19.	Excessively tanned on the face or unable/unlikely to refrain from tanning on the face during the study.
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.

5.2 Subject Numbering

If a subject is willing to participate, provides written informed consent/assent, and meets the study eligibility criteria, the subject will be assigned a study subject identification number. This number is comprised of a site number (which is provided by the Sponsor), a sequential subject number and the subject initials.

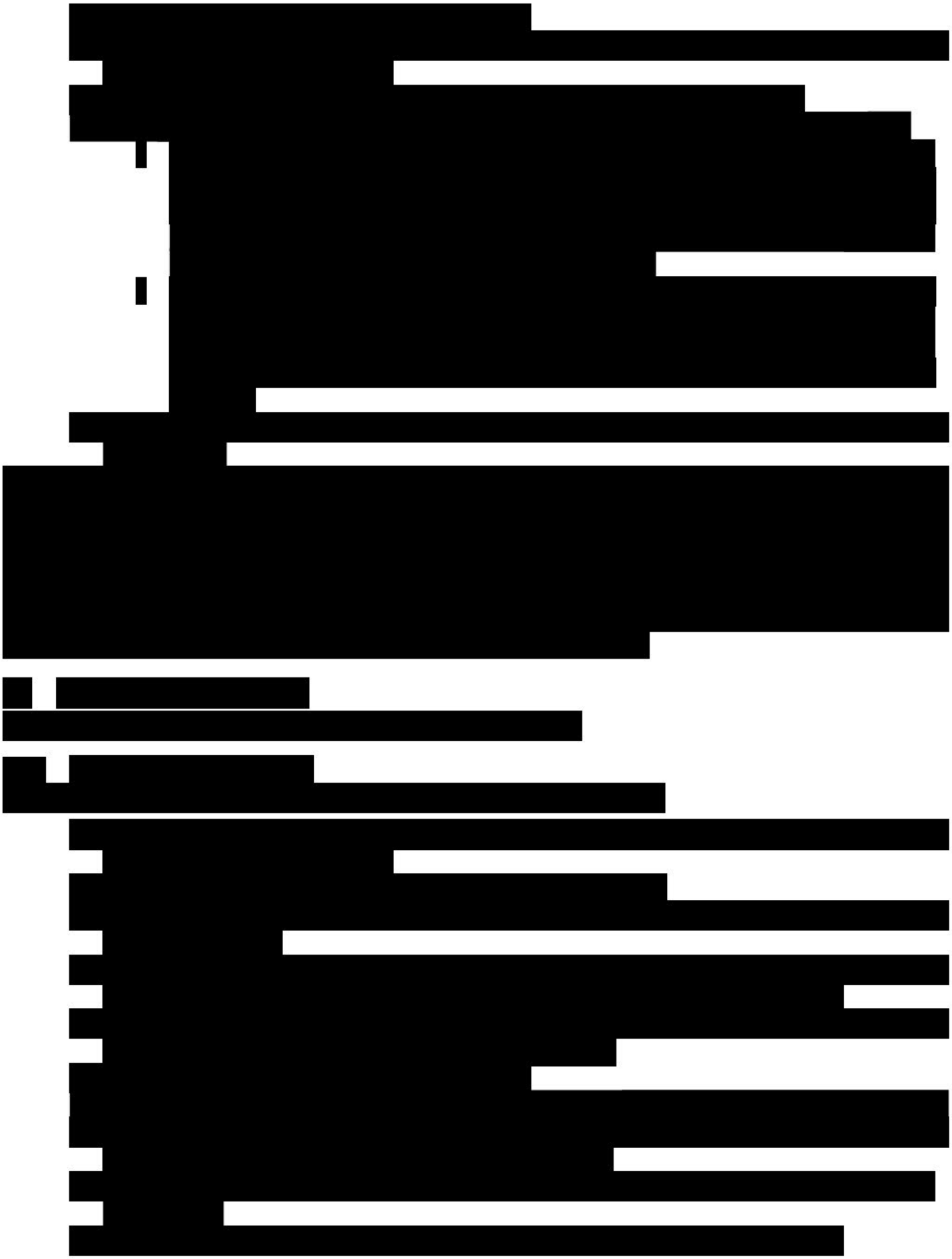
5.3 Subject Discontinuation Criteria

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. 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, including but not limited to: 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.

[redacted]

[redacted]



[redacted]

[redacted]

[redacted]

7.4 Recording AEs/SAEs and ADEs/SADEs

All AEs/SAEs and ADEs/SADEs will be: (1) evaluated, monitored and tracked from the time of the first study treatment and (2) must be recorded in AE section of the protocol specific case report forms (CRFs). Medical occurrences that begin after enrolling into the study and before administration of study treatment will be recorded on the Medical History section of the CRF, not the AE section.

At each contact with the subject, the Investigator must seek information on AEs/ADEs and SAEs/SADEs by specific questioning and, as appropriate, by examination. AEs/ADEs and SAEs/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 CRFs. Included in the description should be the nature of the sign or symptom (including location of the AE/ADE as applicable), 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 the Sponsor as soon as possible (no later than 24 hours after occurrence). The SAE/SADE must be recorded in: (1) the protocol-specific CRF and (2) a written report must be submitted to the Sponsor no later than ten (10) working days after the Investigator first learns of the event. The written report shall include a full description of the event and sequelae, in the format detailed by the Sponsor's SAE/SADE Form. Investigator may be required to submit additional reports to the IRB and to the Sponsor related to SAEs/SADEs.

The Sponsor will immediately conduct an evaluation of any SAE/SADEs per 21 CFR part 812.46(b)(1). If the SAE/SADE is determined to be a USADE, the Sponsor will report results of such evaluation to IRB, FDA and participating Investigators pursuant to 21 CFR part 812.150(b)(1). If the Sponsor determines the USADE presents an unreasonable risk to subjects, the Sponsor will terminate the study or parts of the study presenting that risk pursuant to 21 CFR part 812.46(b)(2).

7.5 Follow-up of Subjects after AEs/ADEs

All reported AEs/ADEs should be followed until resolution. In the unusual circumstance that an AE/ADE has not resolved by the time of the subject's completion of the study, an explanation will be entered on the appropriate CRF and the subject will be referred to his or her primary care provider (unless specified otherwise by the sponsor). Resolutions of events and all events that result in permanent discontinuation from this clinical trial are to be documented on the appropriate CRFs.

7.6 Pregnancy Reporting

Any pregnancy which comes to the attention of the Investigator during the study must be reported to the Sponsor and the IRB as soon as the Investigator or study staff becomes aware of the pregnancy. Subjects who become pregnant during the study will be required to discontinue treatment immediately and be discontinued from the study [redacted] Subject will be followed until completion of pregnancy. Pregnancy itself is not considered an AE/ADE. A congenital anomaly or birth defect will be reported as an SAE.

[redacted]

[redacted]

8.2 Potential Benefits

The subjects may or may not benefit from the study device. Potential benefit of laser treatment is reduction in number and/or severity of acne lesions. There is no guarantee of success.

9 RISK MANAGEMENT

Appropriate risk mitigation measures have been taken to support exposure of these patients to the investigational device, as described below.

The Investigators participating in this study will be chosen based on medical specialty, experience diagnosing and treating acne vulgaris, experience conducting clinical research studies and experience in the use of laser-based devices for aesthetic indications and/or dermatology applications.

In addition, all study Investigators (and qualified designees) will be trained on the use of the investigational Cutera® 1726 nm laser system by a representative of the Sponsor.

[redacted]

11 STATISTICAL CONSIDERATIONS

[redacted]

11.2 Reported Adverse Events

Adverse events (AE) will be categorized as serious and non-serious, device-related and non-device-related, and anticipated and unanticipated. All reported AEs should be followed until resolution. In the unusual circumstance that an AE has not resolved by the time of the subject's completion of the study, an explanation will be entered on the appropriate CRF.

[redacted]

11.3 Primary Effectiveness Endpoint – Percent Change from Baseline in Inflammatory Lesion Counts

Percent Change from Baseline in Inflammatory Lesion Counts (ILC) is calculated as:

$$\frac{100 \times (\text{Follow-Up Visit ILC} - \text{Baseline ILC})}{\text{Baseline ILC}}$$

such that a negative result reflects a decrease in the inflammatory lesion counts, while a positive result reflects an increase. A decrease in the inflammatory lesion counts indicates improvement, therefore negative values reflect improvement.

[redacted]

11.5 Primary and Secondary Safety Analyses

Overall safety of the Cutera® 1726 nm laser system for the treatment of mild to severe acne vulgaris will be assessed by a review of the totality of all reported adverse events.

[redacted]

[redacted]

11.8 Derived Data – Change-from-Baseline Parameters

Within-subject change-from-baseline (pre-treatment baseline) values for a parameter are calculated as:

Change-from-Baseline = Follow-Up value – Pre-Treatment value

such that a negative value indicates a reduction from the pre-treatment value to the follow-up value, whereas a positive result indicates the opposite.

[redacted]

11.10 Statistical Methods

Categorical data will be summarized using frequency tables, presenting the subject counts and relative percentages. McNemar's chi-square may be used to assess within-subject changes in a bivariate response variable.

Continuous variables will be summarized by the mean, standard deviation, median, minimum and maximum. Within-subject changes (Change-from-Baseline) will be analyzed parametrically using the

Paired t-test if the differences are normally distributed, or non-parametrically using the Sign-Rank Test if the differences are not normally distributed. Mid study evaluation of data may be performed to facilitate clinical study report writing. Investigators and panelists will remain blinded to such evaluation.

Appropriate statistical software will be used to perform all analyses. Exact confidence intervals will be generated for estimates of proportions. Asymptotic confidence intervals will be generated for estimates of means. Except where otherwise noted, the p-values of all tests will be reported without any correction for the multiplicity of tests performed.

[redacted]

[redacted]

12 STUDY MANAGEMENT AND ADMINISTRATIVE PROCEDURES

12.1 Training

The Investigator(s) and site research staff will be trained on the study procedures. Sponsor representative(s) may be present at the site during the treatments to ensure that all procedures and documentation are in place.

12.2 Monitoring

Investigator will allow sponsor representatives to periodically review the study documentation. Monitor(s), qualified by training and experience and selected by the Sponsor, will monitor the participating Investigators, investigational sites and study documentation at regular intervals per the Sponsor's standard operating procedures (SOPs), and in compliance with recognized Good Clinical Practices (GCP), FDA's IDE guidance documents, and as outlined in 21 C.F.R. § 812.43(d) and 21 C.F.R. §812.46. The major function of the clinical monitor(s) is to observe and assess compliance of the investigators and investigational sites with the requirements of this clinical study protocol and GCP.

Overall, the monitor's duties include, but are not limited to study site visits and review of clinical study documents and results, which consists of monitoring subject specific consents and case report forms (including source documents as applicable), assessing protocol adherence, ensuring ongoing implementation of required data entry, ensuring ongoing implementation of quality control procedures, and ensuring general adherence to GCP requirements. The monitor(s) will operate under written procedures to ensure compliance with the protocol.

[redacted]

[redacted]

12.3 Informed Consent/Assent

The Investigator is responsible for ensuring that written informed consent, using an FDA and IRB approved informed consent document, is obtained from each subject before the performance of any protocol procedures, including administration of the study device.

The informed consent document must comply with all essential elements as defined in 21 CFR part 50, with consideration given to the guidelines set forth in International Conference on Harmonization (ICH) Good Clinical Practice, the Health Insurance Portability and Accountability Act (HIPAA), as well as other application regulatory requirements and must contain a statement that consent is freely given, the study involves research, the subject is aware of the risks and benefits of entering the study, the subject will be informed of any significant new findings that may affect the subject's willingness to participate in the study and that the subject is free to withdraw from the study at any time. Minor subjects under the age of 18 and one parent or legal guardian must provide written informed consent, including an assent for minors, prior to being enrolled in the study. An evaluation of each candidate will be conducted by the Investigator (or qualified designee). Upon determining a subject's eligibility status, the subject will be offered the opportunity to participate in the study.

12.4 Protocol Compliance

The Investigator must comply with all terms of the protocol.

12.4.1 Protocol Amendments

Neither the Investigator nor the Sponsor will modify, alter, or amend this protocol without first obtaining the concurrence of the other party (with the exception of modifications which involve mitigating a medical emergency or immediate health risk to the subject). IRB and FDA approval must be obtained before implementation of an amendment according to IRB and FDA policies.

12.4.2 Protocol Deviations

All protocol deviations must be clearly described on the appropriate case report form. Deviations from the protocol may include but are not limited to the subject's failure to attend a scheduled visit during a visit window and incomplete or incorrect study procedures. A deviation to protect the life or physical well-being of a subject in an emergency must be reported to the Sponsor as soon as possible (but no later than within 5 working days after the emergency occurred or sooner if required by IRB policies). Except in such an emergency, prior approval by the Sponsor is required for changes in or deviations from a plan. If a deviation does not obtain prior approval from the Sponsor, it must be reported to the Sponsor within 24 hours of the deviation occurring. If a deviation is considered a necessary change to the protocol or likely to reoccur, the Sponsor should initiate an amendment to the protocol to reflect the change. If these changes or deviations have potential to affect the scientific soundness of the plan, the risk/benefit ratio of the study, or the rights, safety or welfare of human subjects, prior approval by FDA and IRB in accordance with 21 CFR 812.35 (a) is also required.

All deviations, including minor or administrative deviations, must be reported to the Sponsor. Significant protocol deviations must be reported to IRB according to their policies.

12.5 Study Personnel

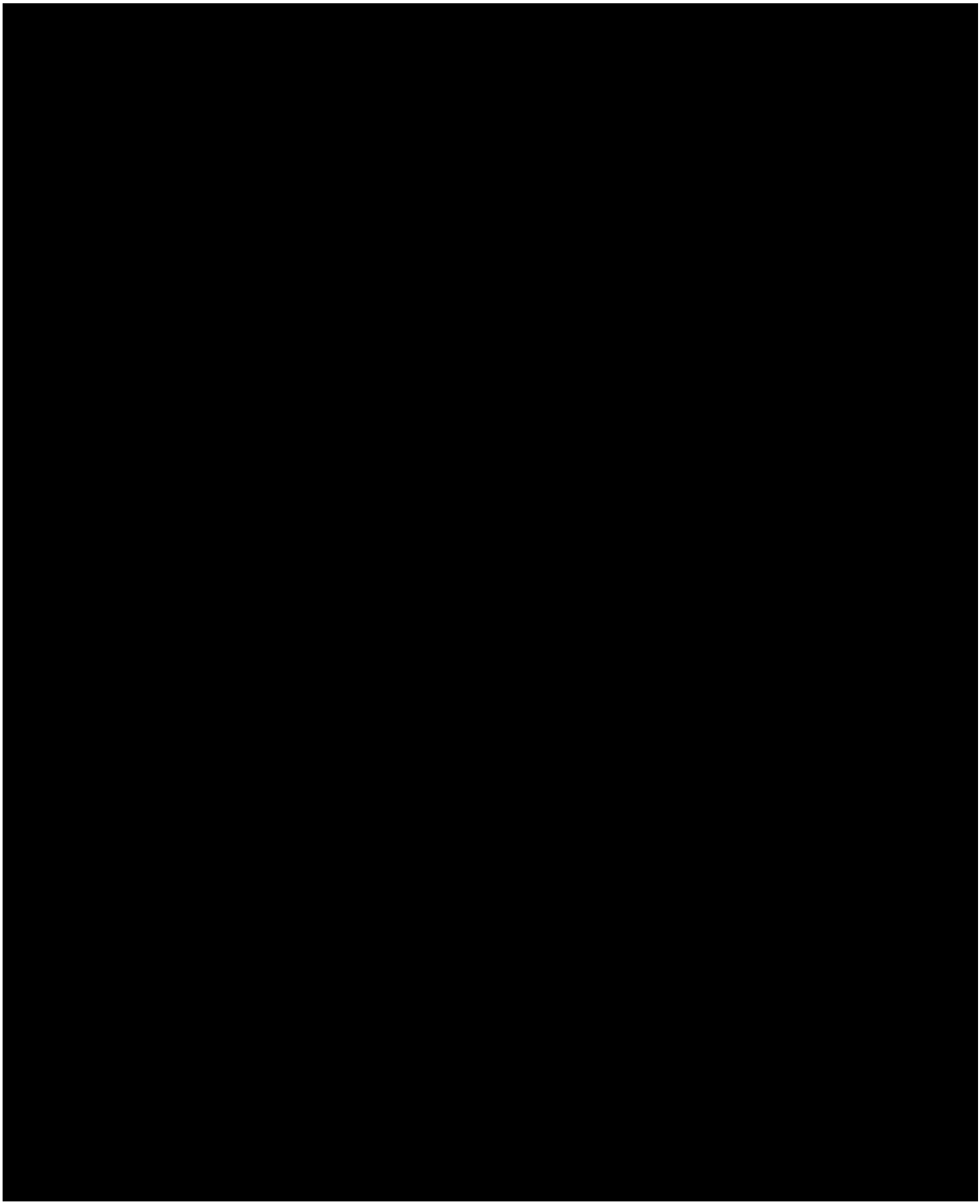
Prior to the start of the study, the Investigator must supply the Sponsor with a list of the names and curricula vitae that describe the professional backgrounds of the clinically responsible study Investigators (principal, sub-investigators), research nurses, coordinators and other possible participants (e.g. medical doctor, nurse, etc.).

12.6 Disclosure of Financial Interest

Each Investigator [principal and sub-investigator(s)] is required to disclose sufficient accurate financial information to the Sponsor on the provided form, to allow sponsor to submit complete and accurate certification or disclosure statements as required under 21 CFR part 54. Each Investigator shall promptly update this information and inform the Sponsor if any relevant changes occur during the course of the study and for 1 year following completion of the study as required under 21 CFR part 812.100(d).

12.7 Clinicaltrials.gov Posting

This study will be posted on clinicaltrials.gov by the Sponsor per the Sponsor's SOP and applicable regulations.



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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:

The subjects will be informed by the Investigator or the qualified designee that their medical records (and other identifying study documents) will be kept as confidential as possible but may be subject to review and copy by: (1) the Sponsor, or its representative; (2) reviewing IRB; and/or (3) by appropriate regulatory bodies (e.g. the US Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies).

[redacted]

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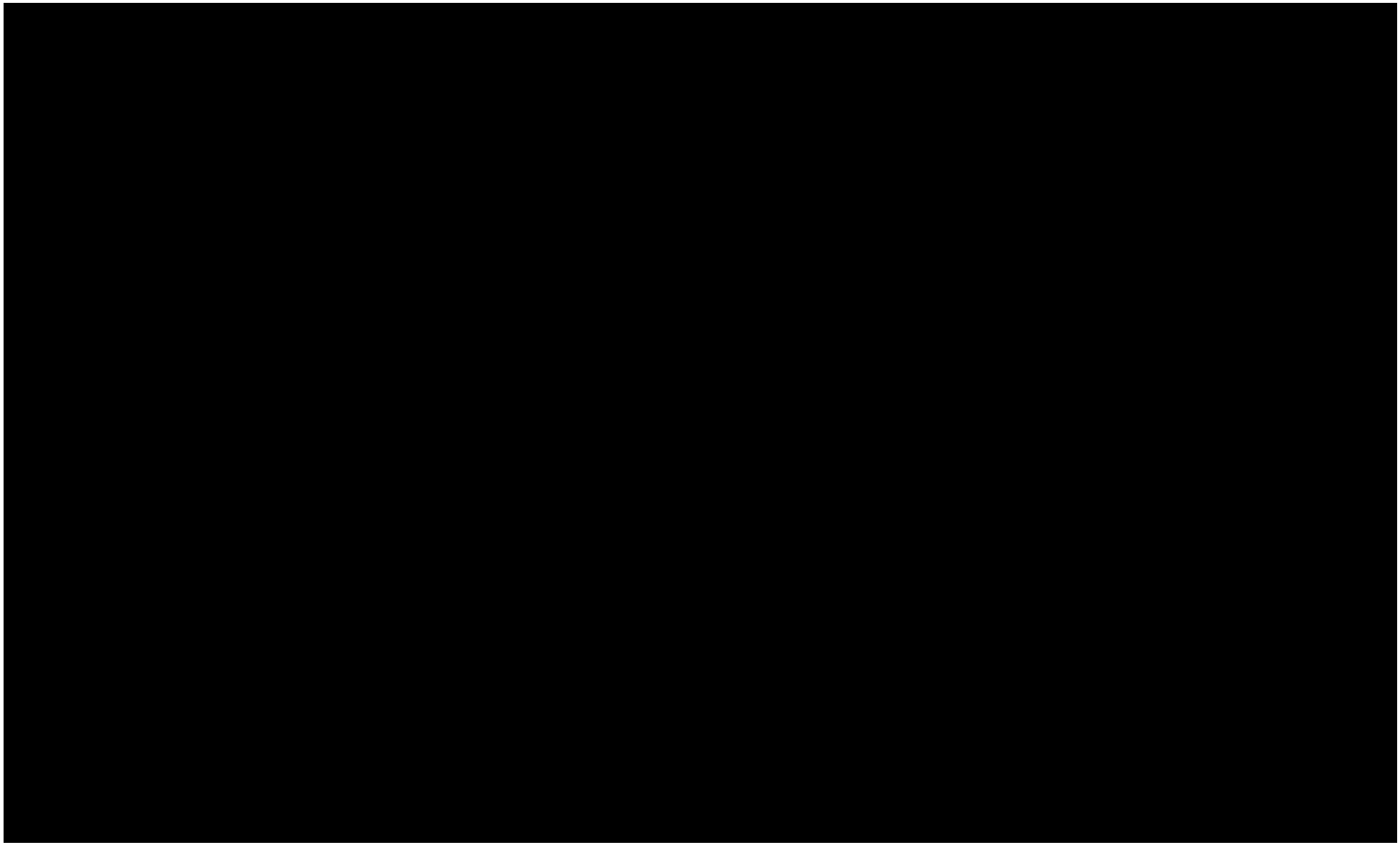

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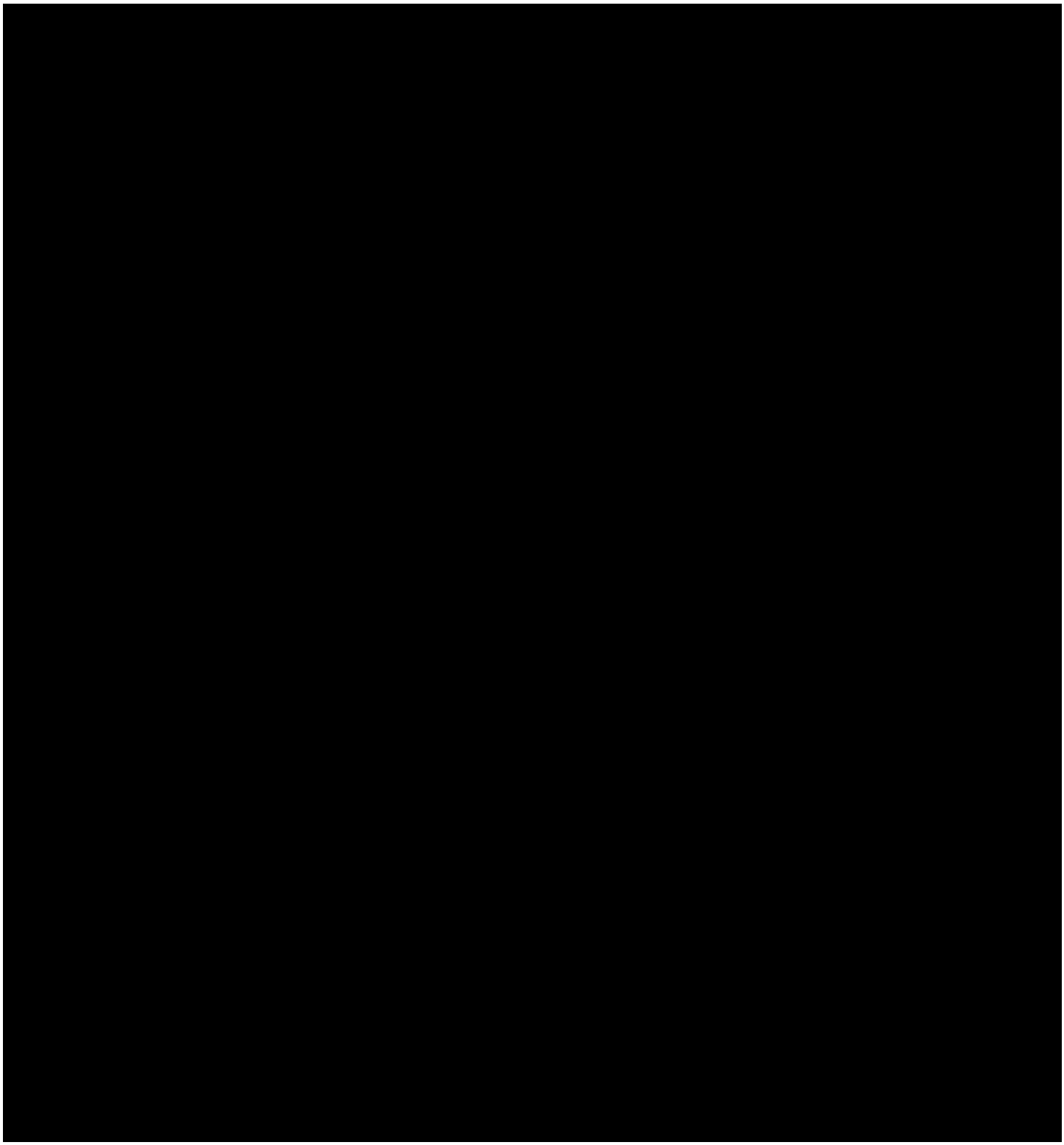

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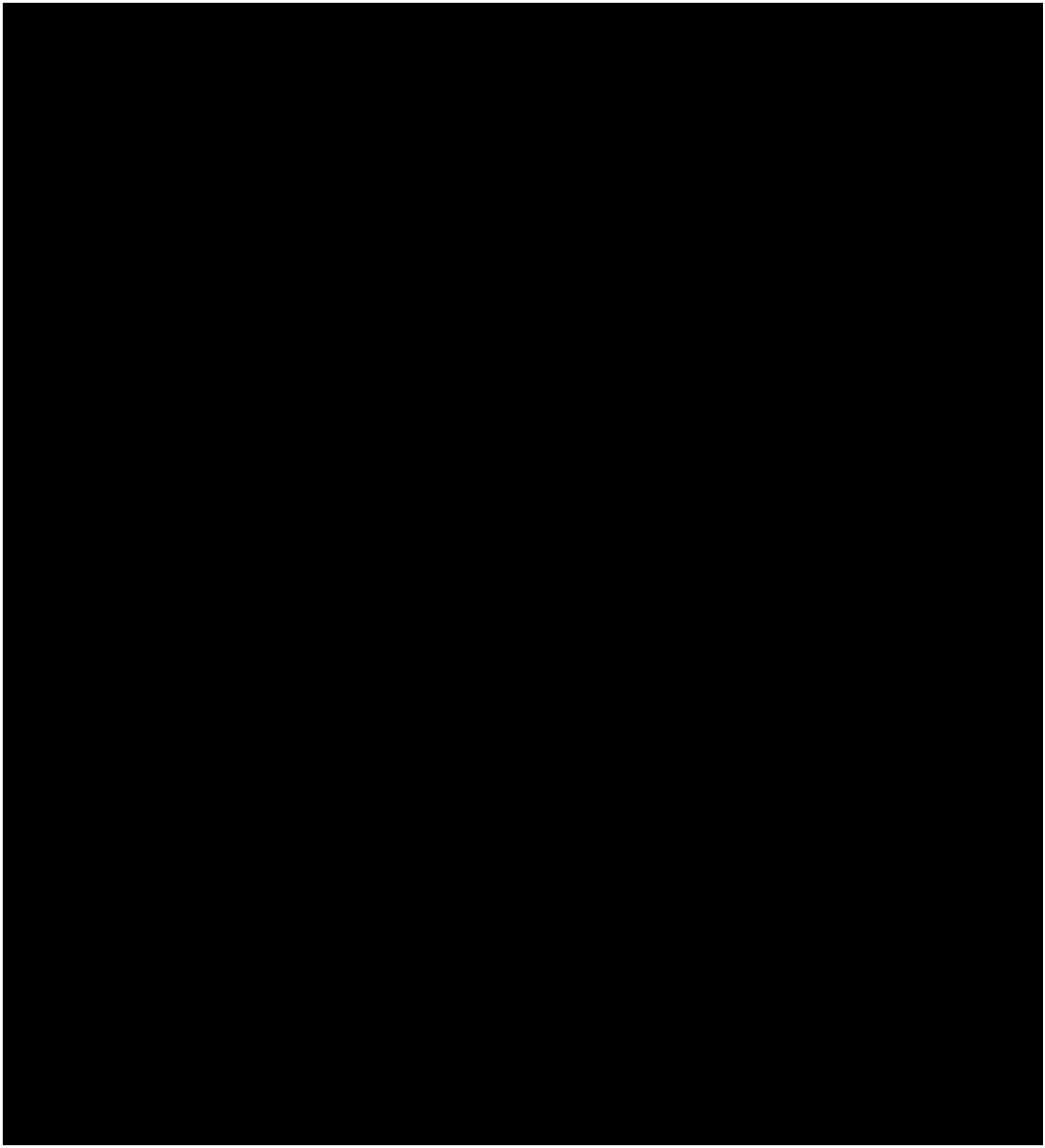

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