Statistical Analysis Plan for Study MED-MA-PLS-0647

CoolSculpting® Elite: Multi-Country Study to Evaluate Patient Satisfaction for Non-Invasive Fat Reduction in Abdomen, Flanks, Upper Arms, Inner Thighs, Outer Thighs and Submental Area [redacted]

Date: 29 July 2022

Version 2.0

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1.0 Introduction

This Statistical Analysis Plan (SAP) describes the statistical analyses for [redacted] Study MED-MA-PLS-0647 CoolSculpting® Elite: Multi-Country Study to Evaluate Patient Satisfaction for Non-Invasive Fat Reduction in Abdomen, Flanks, Upper Arms, Inner Thighs, Outer Thighs and Submental Area [redacted]. Specifications of tables, figures, and data listings are contained in a separate document.

Study MED-MA-PLS-0647 is a global, multicenter, multi-country, prospective, open-label, nonrandomized, interventional cohort, medical device post-marketing study evaluating the use of CoolSculpting Elite and CoolSculpting Elite applicators for noninvasive subcutaneous fat reduction of the abdomen and flanks in healthy volunteers, as well as also consider treatment of the upper arms, inner thighs, outer thighs, and submental area. Participants will be enrolled at approximately 9 study sites. Approximately 110 participants will be enrolled and approximately 96 participants are expected to complete the primary endpoint assessment based on an anticipated attrition rate of 12% or less.

The study duration is up to approximately 20 weeks and consists of up to 7 scheduled study visits and 2 phone follow-ups per participant. Signed informed consent from the participants will be obtained before any study-related procedures are performed. Participants meeting the inclusion criteria will be assigned to receive up to 2 treatment sessions separated at least 8 weeks apart for the body areas eligible for treatment. Assessments will be completed 12 weeks after the final treatment session (measured at week 12 for participants who receive 1 treatment session to a specific body area, or week 20 for participants who receive 2 treatment sessions to a specific body area).

If a participant receives one treatment session to a specific body area and two treatment sessions to another specific body area, the participant will return for both 12-week follow-up visits: Visit 8 (week 12) for the 12-week post-treatment session 1 assessment of the body area that received only one treatment session and Visit 9 (week 20) for the 12-week post treatment session 2 assessment of the body area receiving two treatment sessions; Visit 9 (week 20) will also be the study exit visit for this participant.

For those participants who could not receive or complete their second treatment session (Visit 6) prior to the temporary hold on CoolSculpting® Elite treatment in the US on / after 24th August 2021, these participants will be rescheduled for their second treatment session (Visit 6) within 6 weeks following communication from the sponsor that CoolSculpting® Elite treatment could recommence in the study.

Participants withdrawing from the study will be encouraged to complete the same final evaluations as participants completing the study according to this protocol, particularly safety evaluations.

The SAP will not be updated in case of administrative changes or amendments to the protocol unless the changes impact the analysis.

Unless noted otherwise, all analyses will be performed using SAS Version 9.4 (SAS Institute Inc., Cary, NC 27513) or later.

2.0 Study Design and Objectives

2.1 Objectives, Hypotheses and Estimands

The objectives include:

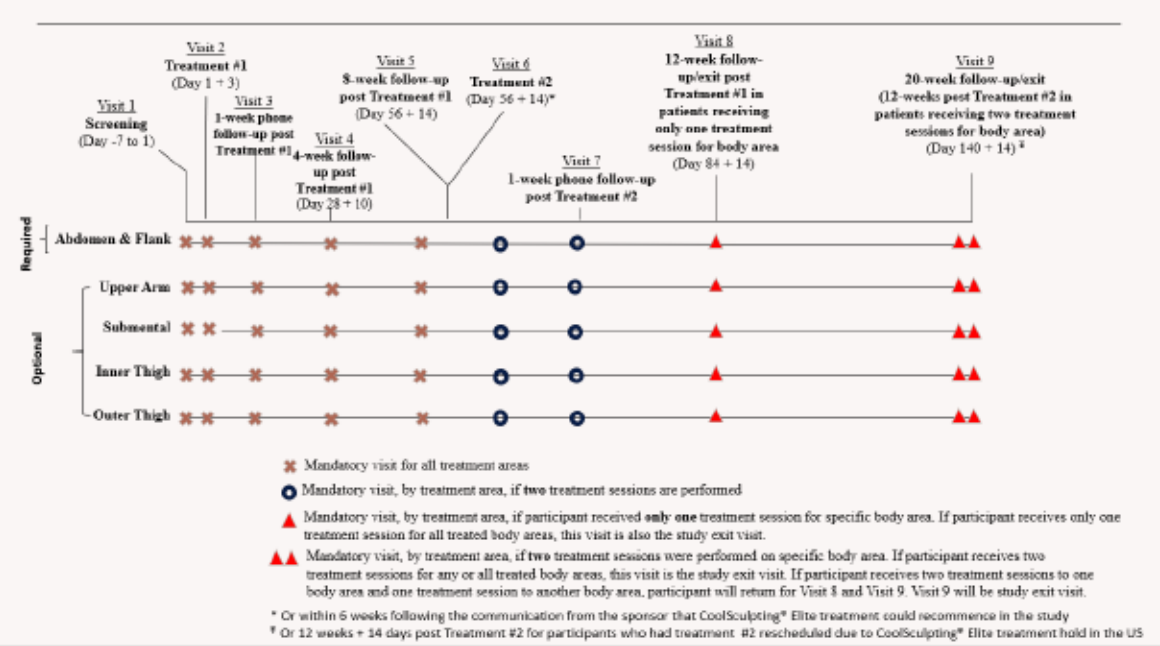
- To evaluate participant satisfaction and effectiveness of the CoolSculpting Elite System using CoolSculpting Elite applicators for non-invasive subcutaneous fat reduction of the abdomen and flanks, upper arms, inner thighs, outer thighs and submental area
- To evaluate safety of the CoolSculpting Elite System using CoolSculpting Elite applicators for non-invasive subcutaneous fat reduction of the abdomen and flanks, upper arms, inner thighs, outer thighs and submental area

No statistical hypotheses are planned to be tested.

2.2 Study Design Overview

The schematic of the study is shown in Figure 1.

Figure 1. Study Schematic



The schedule of activities is shown in Table 1.

Table 2. Schedule of Activities

Evaluations	Visit 1 Screening	Visit 2 Treatment Session #1	Visit 3 1-week Phone Follow-up [1a,b]	Visit 4 4-week Follow-up	Visit 5 8-week Follow-up	Visit 6 Treatment Session #2	Visit 7 1-week Phone Follow-up[2a,b]	Visit 8 12-week Follow-up/Exit for participants who received only 1 treatment session[3]	Visit 9 20-week (12-week Follow-up/ Exit for participants who received 2 treatment sessions)[3]	Notes
Visit Window	Day -7 to 1	Day 1 + 3		Day 28 + 10	Day 56 + 14	Day 56 + 14 (or within 6 weeks following the communication from the sponsor that CoolSculpting® Elite treatment could recommence in the study)		Day 84 + 14	Day 140 + 14 (or 12 weeks +14 days post treatment session 2 for those participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US)	
Visit Notes	Mandatory for all treatment areas	Mandatory for all treatment areas	Mandatory for all treatment areas	Mandatory for all treatment areas	Mandatory for all treatment areas.	Mandatory, by treatment area, if two treatment sessions. May occur same day as Visit 5.*	Mandatory, by treatment area, if two treatment sessions	Mandatory, by treatment area, if only one treatment session	Mandatory, by treatment area, if two treatment sessions	See Protocol Section 7.2 for detail on information to be captured in Visit in case of study discontinuation
Informed Consent	X									
Inclusion/ Exclusion	X	X		X	X	X		X	X	See Protocol Sections 5.1 and 5.2
Demographics	X									

Evaluations	Visit 1 Screening	Visit 2 Treatment Session #1	Visit 3 1-week Phone Follow-up [1a,b]	Visit 4 4-week Follow-up	Visit 5 8-week Follow-up	Visit 6 Treatment Session #2	Visit 7 1-week Phone Follow-up [2a,b]	Visit 8 12-week Follow-up/Exit for participants who received only 1 treatment session[3]	Visit 9 20-week (12-week Follow-up/ Exit for participants who received 2 treatment sessions)[3]	Notes
Medical/ Surgical History	X									
Concomitant Medications and procedures	X	X	X	X	X	X	X	X	X	See Protocol Section 6.5.1. At Visits 2 and 6, repeat if participant is treated over multiple days with > 24 hours between treatments.
Review Contraceptive Guidance	X	X	X	X	X	X	X	X	X	See Protocol Section 10.4, for WOCBP
Urine Pregnancy Test	X	X				X				See Protocol Section 8.2.3, conduct before cryo-lipolysis treatments at Visits 2 and 6. At Visits 2 and 6, repeat if participant is treated over multiple days with > 24 hours between treatments.
Treatment site assessment		X		X	X	X		X	X	Conduct after cryo-lipolysis

Evaluations	Visit 1 Screening	Visit 2 Treatment Session #1	Visit 3 1-week Phone Follow-up [1a,b]	Visit 4 4-week Follow-up	Visit 5 8-week Follow-up	Visit 6 Treatment Session #2	Visit 7 1-week Phone Follow-up [2a,b]	Visit 8 12-week Follow-up/Exit for participants who received only 1 treatment session[3]	Visit 9 20-week (12-week Follow-up/ Exit for participants who received 2 treatment sessions)[3]	Notes
										treatments and prior to massage at Visits 2 and 6.
Height	X									
Weight	X	X		X	X			X	X	Conduct before cryo-lipolysis treatments at Visits 2 and 6.
2D/3D Photography[4]	X	X		X	X			X	X	See Protocol Section 8.1.2, conduct before cryo-lipolysis treatment at Visits 2 and 6
Cryolipolysis Treatment		X				X				See Protocol Section 6
Pain Assessment		X	X	X	X	X	X	X	X	See Protocol Section 8.2.1
AE, SAE, ADE, SADE	X	X	X	X	X	X	X	X	X	At Visits 2 and 6, repeat if participant is treated over multiple days with > 24 hours between treatments.
Device Complaint Query		X	X	X	X	X	X	X	X	At Visits 2 and 6, repeat if participant is treated over multiple days with > 24 hours

Evaluations	Visit 1 Screening	Visit 2 Treatment Session #1	Visit 3 1-week Phone Follow-up [1a,b]	Visit 4 4-week Follow-up	Visit 5 8-week Follow-up	Visit 6 Treatment Session #2	Visit 7 1-week Phone Follow-up[2a,b]	Visit 8 12-week Follow-up/Exit for participants who received only 1 treatment session[3]	Visit 9 20-week (12-week Follow-up/ Exit for participants who received 2 treatment sessions)[3]	Notes
										between treatments.
CSQ [6 versions][5]					X			X	X	See Protocol Section 10.6-10.11
CGPQ[6]								X	X	See Protocol Section 10.12
CPIQ[7]		X			X			X	X	See Protocol Section 10.13 Complete before cryolipolysis treatment at Visit 2.
Participant Evaluation of Noticeable Improvement				X						See Protocol Section 10.15
[redacted]								X	X	[redacted]

[1a] Phone follow-up should be scheduled 7 days from last treatment visit day in instance where participant received treatment session #1 over multiple days.

[1b] If, during this phone follow-up, any of the following local effects of erythema, bruising, swelling, and/or sensory alteration are reported related to treatment session #1, additional phone follow-up (or in-person visit if aligned to planned study visit) will be scheduled in accordance with the time criteria outlined in Table 2-1 for potential AE categorization.

[2a] Phone follow-up should be scheduled 7 days from last treatment visit day in instance where participant received treatment session #2 over multiple days.

[2b] If, during this phone follow-up, any of the following local effects of erythema, bruising, swelling, and/or sensory alteration are reported related to treatment session #2, additional phone follow-up (or in-person visit if aligned to planned study visit) will be scheduled in accordance with the time criteria outlined in Table 2-1 for potential AE categorization.

[3] If a participant receives only one treatment session for specific body area(s), the participant will return at Visit 8 for the 12-week post-treatment session #1 follow up assessment and study exit. If a participant receives two treatment sessions to any or all treated body areas, participant will return at Visit 9 for 12-week post-treatment session #2 follow-up and study exit. If a participant receives only one treatment session to one specific body area and two treatment sessions to another specific body area, the participant will return for Visit 8 for 12-week follow-up for the body area that received only one treatment session and Visit 9 for 12-week follow-up of body area that received two treatment sessions. The exit for this participant is Visit 9.

[4] For select study sites with 3D camera system, 3D images will also be taken at this time.

[5] CSQ-Overall is to be administered only if patient received treatment to midsection (abdomen and flank) plus at least one additional specific body area. The CSQ-Overall should be completed at visit where at least 12-weeks have passed since the final treatment session for all the treated body areas. For example, if the participant receives only one treatment session for one specific body area but two treatment sessions for another specific body area, the CSQ-Overall should be administered at Visit 9 where all the treated body areas will have undergone at least a 12-week post treatment period.

[6] The CGPQ should be completed at visit where at least 12-weeks have passed since the final treatment session for all the treated body areas. For example, if the participant receives only one treatment session for one specific body area but two treatment sessions for another specific body area, the CGPQ should be administered at Visit 9 where all the treated body areas will have undergone at least a 12-week post treatment period.

[7] The 12-week post final treatment CPIQ should be completed at visit where at least 12-weeks have passed since the final treatment session for all the treated body areas. For example, if the participant receives only one treatment session for one specific body area but two treatment sessions for another specific body area, the CPIQ should be administered at Visit 9 where all the treated body areas will have undergone at least a 12-week post treatment period.

* Option for Visit 5 and Visit 6 to occur same day only applies if participant received treatment session #2 prior to temporary hold on CoolSculpting Elite hold on CoolSculpting® Elite treatment in the US on / after 24th August 2021.

2.3 Treatment Assignment and Blinding

Study intervention is defined as the medical device (CoolSculpting Elite System and CoolSculpting Elite applicators) intended to be administered to a study participant according to the study protocol.

At screening, after the participant has signed the informed consent form (ICF), the participant will be assigned a screening number sequentially based on the order in which the participant is screened into the study at that particular site. The participant identification number (i.e., site ID concatenated with the participant screening number) will serve as the participant identification number on all study documents.

Participants will undergo a CoolSculpting Elite treatment in an outpatient clinical setting. A treatment is comprised of timed segments of cooling (treatment cycle) followed by 2 minutes of manual massage. Treatments will be administered according to the CoolSculpting Elite user manual that has been prepared for specific countries and provided to the study sites. The CoolSculpting Elite applicators available in this study depend on country clearances and can include Curve 240, Curve 150, Curve 120, Flat 165, Flat 125, Surface 150, and Curve 80.

Blinding is not applicable to this open-label, nonrandomized study. Blinding will only be employed for photograph review by an independent panel of physician reviewers with expertise in the areas of dermatology and/or plastic surgery.

2.4 Sample Size Determination

The sample size was planned to provide reasonable precision for the estimate of the primary effectiveness endpoint, overall satisfaction rate for the midsection of the various body areas treated with CoolSculpting.

Previous studies conducted on participants undergoing flank or abdominal fat reduction using the CoolSculpting device reported moderately high overall satisfaction rate. [redacted] A sample size of 96 participants would provide a two-sided 95% confidence interval (CI) with a width equal to 0.2 when the overall satisfaction rate is 63.9%. Exact (Clopper-Pearson) method from the commercial software PASS 2008 was used for the sample size calculation. Allowing for a 12% attrition rate during the study period, approximately 110 participants will be needed for recruitment into the study.

If local guidelines are in effect to prevent and mitigate the effects of a pandemic or natural disaster, it is possible that some participants may not be able to complete all site visits as indicated per protocol. To preserve the sample size calculation, additional participants may be enrolled if more than 12% of the participants fail to complete the Cryolipolysis Satisfaction Questionnaire (CSQ)-Midsection Item 1 at 12 weeks after the final treatment.

3.0 Endpoints

3.1 Primary Effectiveness Endpoint

The primary effectiveness endpoint is the proportion of participants with "satisfied" or "very satisfied" on the Item 1 for the CSQ-Midsection, measured at 12-week follow-up of final treatment [Week 12 (Visit 8) for participants who receive 1 treatment session, or Week 20 (Visit 9) for participants who receive 2 treatment sessions, or 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021].

3.2 Secondary Effectiveness Endpoints

The secondary effectiveness endpoints include:

- The proportion of participants who received treatment to abdomen and flank and one or more additional body areas for treatment with "satisfied" or "very satisfied" on CSQ-Overall Item 1 measured at 12-week follow-up of final treatment [Week 12 (Visit 8) for participants who receive only 1 treatment session to all treated body areas, or Week 20 (Visit 9) for participants who receive 2 treatment sessions to any or all treated body areas, or 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021].

- The proportion of participants with "satisfied" or "very satisfied" on individual treated body area (upper arms, inner thighs, outer thighs, fat under chin) CSQ Item 1 measured at 12-week follow-up of final treatment [Week 12 (Visit 8) for participants who receive only 1 treatment session, or Week 20 (Visit 9) for participants who receive 2 treatment sessions, or 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021] for the respective treated body areas.

If local guidelines are in effect to prevent and mitigate the effects of a pandemic or natural disaster, it is possible that some participants may not be able to complete all site visits as indicated per protocol. To preserve the sample size calculation, additional participants may be enrolled if more than 12% of the participants fail to complete the Cryolipolysis Satisfaction Questionnaire (CSQ)-Midsection Item 1 at 12 weeks after the final treatment.

3.0 Endpoints

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3.2 Secondary Effectiveness Endpoints

The secondary effectiveness endpoints include:

- The proportion of participants who received treatment to abdomen and flank and one or more additional body areas for treatment with "satisfied" or "very satisfied" on CSQ-Overall Item 1 measured at 12-week follow-up of final treatment [Week 12 (Visit 8) for participants who receive only 1 treatment session to all treated body areas, or Week 20 (Visit 9) for participants who receive 2 treatment sessions to any or all treated body areas, or 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021].

- The proportion of participants with "satisfied" or "very satisfied" on individual treated body area (upper arms, inner thighs, outer thighs, fat under chin) CSQ Item 1 measured at 12-week follow-up of final treatment [Week 12 (Visit 8) for participants who receive only 1 treatment session, or Week 20 (Visit 9) for participants who receive 2 treatment sessions, or 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021] for the respective treated body areas.

- Correct identification of baseline vs 12-week follow-up of final treatment [Week 12 (Visit 8) for participants who receive only 1 treatment session, or Week 20 (Visit 9) for participants who receive 2 treatment sessions, or 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021] images of the treated body area(s) by at least two out of three blinded, independent reviewers for the following body areas:

  - Midsection
  - Upper arms
  - Inner thighs
  - Outer thighs
  - Submental area

  Success will be defined as at least 70% correct identification of the pre-treatment images.

3.3 Exploratory Effectiveness Endpoints

The exploratory effectiveness endpoints include:

- [redacted]

3.4 Safety Endpoints

- Adverse events (AEs) and adverse device effects (ADEs); serious adverse events (SAEs), serious adverse device effects (SADEs)
- Unanticipated AEs or ADEs (including Unanticipated SAE/SADEs)
- Pain assessments (0 to 10 scale, 0=no pain and 10=the worst pain imaginable)
- Post-treatment clinical assessment – epidermal, dermal, or subcutaneous findings
- Post-treatment clinical assessment – alteration in sensation
- Medical device deficiencies

4.0 Analysis Populations

The following population sets will be used for the statistical analyses.

The Enrolled Population will consist of all participants who signed the informed consent.

The Safety Population will consist of all enrolled participants who received at least one cryolipolysis treatment cycle (started or completed).

The Evaluable Population 1 will consist of all participants who completed the cryolipolysis treatment plan to the midsection and completed the CSQ-Midsection Item 1 at 12 weeks after the final treatment measured at Visit 8 (Week 12) for participants who receive 1 treatment session, or at Visit 9 (Week 20) for participants who receive 2 treatment sessions, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021, and do not have any significant protocol deviation or violation.

The Evaluable Population 2 will consist of all participants who completed the cryolipolysis treatment plan for any other body areas (Upper Arms, Inner Thighs, Outer

Thighs and Submental Area) whether midsection treatment is completed or not, and do not have any significant protocol deviation or violation .

The Evaluable Population 3 will consist of all participants who completed the cryolipolysis treatment plan for any body areas (Midsection, Upper Arms, Inner Thighs, Outer Thighs and Submental Area) and do not have any significant protocol deviation or violation.

The Evaluable Population 4 will consist of all participants who completed the cryolipolysis treatment plan to the midsection and one or more additional body areas (Upper Arms, Inner Thighs, Outer Thighs and Submental Area) and do not have any significant protocol deviation or violation.

5.0 Participant Disposition

The number of participants who are in the Enrolled Population and the number and percentage of participants who are in the Safety Population, Evaluable Population 1, Evaluation Population 2, Evaluable Population 3, and Evaluable Population 4 will be summarized. Under Evaluable Population 2, the number and percentage of participants who completed each individual treated body area (Upper Arms, Inner Thighs, Outer Thighs and Submental Area) will be summarized. The number and percentage of screen failure participants and the screen failure reasons will also be summarized for the Enrolled Population.

The number and percentage of participants who complete the study and who prematurely discontinue from study will be presented for the Safety Population; furthermore, the number and percentage of participants discontinued prematurely from study will be presented for the Safety Population by the primary reason for discontinuation as collected on the eCRF. Reasons for premature discontinuation from the study include:

- Adverse Event
- Withdrawal of consent
- Pregnancy
- Protocol Deviation
- PI Discretion
- Chronic Disease (for EU only)

- Lost to follow-up
- Other

A Listing of participant disposition will be provided for the Enrolled Population.

6.0 Treatment Exposure and Compliance

The total number of completed treatment cycles will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum and maximum) for combined treated body areas, by each treatment session and overall for the Safety Population, Evaluable Population 1, Evaluable population 2, Evaluable Population 3, and Evaluable Population 4. Combined treated body areas including combined upper and lower abdomens, combined right and left flanks, combined upper and lower abdomens and right and left flanks, combined right and left upper arm, combined right and left inner thigh, combined right and left outer thigh, and all combined treated body areas. The average percentage of overlapping treatment on each body area will be listed but not summarized.

The number and percentage of treatments interrupted or discontinued along with the reason will be presented for individual treated body area, and for combined treated body areas as specified in Section 6.0, by treatment session and overall for the Safety Population.

The number and percentage of participants with single, dual, triple, or quad applicators used will be summarized by country, treatment session and overall for the Safety Population.

The completed treatment plan will be summarized by country, treatment round, treatment session and overall for the Safety Population.

The study investigators are responsible for performing the study in compliance with the protocol. The treatment compliance will not be applicable in the study.

All treatment exposure data will be listed for the Safety Population.

7.0 Demographics, Baseline Characteristics, Medical History, and Prior/Concomitant Medications

7.1 Demographics and Baseline Characteristics

Demographic parameters will be summarized descriptively for the Safety Population, Evaluable Population 1, and Evaluable Population 2. Demographic parameters include age, sex (if female, childbearing potential), race, and ethnicity, where race and ethnicity are collected only at sites in US and Singapore. Demographic parameters will also be summarized descriptively by treated body area for the Evaluable Population 3.

Baseline characteristics will be summarized descriptively for the Safety Population, Evaluable Population 1, and Evaluable Population 2. Baseline characteristics include weight, height, Fitzpatrick Skin Type (I, II, III, IV, V, VI), and body mass index (BMI). Baseline characteristics will also be summarized descriptively by treated body area for the Evaluable Population 3.

Demographic and baseline characteristics will be provided in a listing for the Safety Population.

7.2 Medical, Surgical and/or Cosmetic History

Medical, surgical and/or cosmetic procedural history data will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The actual version of the MedDRA will be noted in the statistical tables and clinical study report. The number and percentage of participants in each system organ class (SOC) and preferred term (PT) will be summarized for the Safety Population.

The summary table by SOC and PT will be presented with SOC in alphabetical order and PT in decreasing frequency within each SOC. If more than one medical history term is coded to the same PT for the same participant, the participant will be counted only once for that PT.

A listing will be provided for the Safety Population.

7.3 Prior and Concomitant Medications

A prior medication is defined as any medication that started and stopped prior to the date of the first CoolSculpting Elite procedure.

A concomitant medication is defined as any medication that started prior to the date of the first CoolSculpting Elite procedure and continued after the first CoolSculpting Elite procedure, or any medication that started on or after the date of first CoolSculpting Elite procedure.

Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary (WHO DD). The actual version of the WHO DD will be noted in the statistical tables and clinical study report.

The number and percentage of participants with use of prior and concomitant medications will be summarized separately, by anatomic therapeutic chemistry (ATC) class and PT for the Safety Population. The summary will be presented with ATC class in alphabetical order and PT in decreasing frequency within each ATC class. If a participant took a specific medication multiple times or took multiple medications within a specific PT, that participant would be counted only once for the PT.

A listing will be provided for the Safety Population.

7.4 Concomitant Procedures

All concomitant procedures will be listed for the Safety Population.

7.5 Protocol Deviations and Violations

A protocol deviation (PD) is any non-adherence to study procedures that does not result in additional risk to the participant. Protocol deviations will be reviewed and documented before database lock.

A protocol violation (PV) is any non-adherence to the protocol that may result in significant additional risk to the participant (eg, enrollment of a participant who does not meet the study criteria). A protocol violation can also be an event of non-adherence to GCPs that may impact participant safety (eg, failure to obtain proper consent before performing study procedures). Violations should be reported to the study sponsor and the IRB within 5 working days if they occur.

Significant PDs/PVs (equivalent to major PDs/PVs as collected in data) listed below will be identified before database lock. The number and percentage of participants with significant PDs/PVs will be summarized for the Safety Population. Significant PDs/PVs related to the following categories which impact the study conduct, data validity or integrity for the study outcomes will be included:

- Key inclusion criteria

- Key exclusion criteria
- Withdrawal criteria
- Treatment
- Concomitant medications
- Timeframe deviation

A listing will be provided for the Enrolled Population.

8.0 Handling of Potential Intercurrent Events for the Primary and Key Secondary Endpoints

Not applicable.

9.0 Effectiveness Analyses

9.1 General Considerations

All effectiveness analyses will be conducted in the Evaluable Population 1, 2, 3 and 4. Baseline for effectiveness is defined as the last non-missing effectiveness assessment before the first Coolsculpting procedure. All Confidence Intervals (CIs) will be 2-sided 95% CIs, unless stated otherwise.

The summaries will be provided by participants with 1 treatment session, participants with 2 treatment sessions and overall, where applicable.

9.2 Handling of Missing Data

No imputation of missing data will be made for any effectiveness analysis.

9.3 Primary Effectiveness Endpoint(s) and Analyses

9.3.1 Primary Effectiveness Endpoint(s)

The primary effectiveness endpoint of this study is the proportion of participants with "satisfied" or "very satisfied" on the Item 1 for the CSQ-Midsection, measured at Week 12 (Visit 8) for participants who receive 1 treatment session, or at Week 20 (Visit 9) for participants who receive 2 treatment sessions, or at 12 weeks +14 days post treatment

session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021.

9.3.2 Main Analysis of Primary Effectiveness Endpoint(s)

The CSQ consists of 6 versions: CSQ-Midsection, CSQ-Overall, CSQ-Upper Arms, CSQ-Inner Thighs, CSQ-Outer Thighs, CSQ-Fat under chin. However, only CSQ-Midsection will be used for the primary analysis. In each version, the CSQ Item 1 is about rating the participant overall satisfaction with the results of the fat reduction procedure on the treated body area based on the following categories:

- Very satisfied
- Satisfied
- Neither satisfied nor dissatisfied
- Dissatisfied
- Very dissatisfied

The number and percentage of participants with "satisfied" or "very satisfied" on the Item 1 for the CSQ-Midsection at Week 12 (Visit 8) for participants who receive 1 treatment session, or at Week 20 (Visit 9) for participants who receive 2 treatment sessions, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021 will be summarized for the Evaluable Population 1 and the two-sided Fisher's exact 95% CI on the percentage will be provided.

A listing will be provided for CSQ-Midsection for the Safety Population.

9.3.3 Sensitivity and Supplementary Analyses of the Primary Effectiveness Endpoint(s)

Not applicable.

9.4 Secondary Effectiveness Endpoints and Analyses

9.4.1 Key Secondary Effectiveness Endpoints

The key secondary effectiveness endpoints include:

- The proportion of participants who received treatment to abdomen and flank and one or more additional body areas for treatment with "satisfied" or "very satisfied" on CSQ-Overall Item 1 measured at Week 12 (Visit 8, 12-week follow-up) for participants who receive only 1 treatment session to all treated body areas, or at Week 20 (Visit 9, 12-week follow-up) for participants who receive 2 treatment sessions to any or all treated body areas, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021.

- The proportion of participants with "satisfied" or "very satisfied" on individual treated body area (upper arms, inner thighs, outer thighs, fat under chin) CSQ Item 1 measured at Week 12 (Visit 8, 12-week follow-up) for participants who receive only 1 treatment session, or at Week 20 (Visit 9, 12-week follow-up) for participants who receive 2 treatment sessions for the respective treated body areas, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021.

- Correct identification of baseline vs 12-week post-final treatment images of the treated body area(s) by at least two out of three blinded, independent reviewers for the following body areas:

    - Midsection
    - Upper arms
    - Inner thighs
    - Outer thighs
    - Submental area

  Success will be defined as at least 70% correct identification of the pre-treatment images.

9.4.2 Main Analyses of Key Secondary Effectiveness Endpoints

The number and percentage of participants with "satisfied" or "very satisfied" on the Item 1 for the CSQ-Overall, CSQ-Upper Arms, CSQ-Inner Thighs, CSQ-Outer Thighs and CSQ-Fat Under Chin, at Week 12 (Visit 8) for participants who receive 1 treatment session, or at Week 20 (Visit 9) for participants who receive 2 treatment sessions, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021 will be summarized for the Evaluable Population 4 (overall) and Evaluable

Population 2 (other treated body areas) and the two-sided Fisher's exact 95% CI on the percentage will be provided.

The number and percentage of participants with correct identification of baseline vs 12-week post-final treatment by 2/3 and 3/3 blinded, independent reviewers for the following body areas will be summarized for the Evaluable Population 1 (midsection) and Evaluable Population 2 (other treated body areas) and the two-sided Fisher's exact 95% CI on the percentage will be provided:

- Midsection
- Upper arms
- Inner thighs
- Outer thighs
- Submental area

Listings will be provided for CSQ-Overall, CSQ-Upper Arms, CSQ-Inner Thighs, CSQ-Outer Thighs and CSQ-Fat Under Chin, and correct identification of baseline vs 12-week post-final treatment for the Safety Population.

9.4.3 Sensitivity and Supplementary Analyses for Key Secondary Effectiveness Endpoints

Not applicable.

9.4.4 Supportive Secondary Effectiveness Endpoints and Analyses

Not applicable.

9.5 Exploratory Effectiveness Endpoints and Analyses

9.5.1 Exploratory Effectiveness Endpoints

The exploratory effectiveness endpoints include:

- [redacted]

- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
  - [redacted]
  - [redacted]
- [redacted]

9.5.2 Main Analysis of Exploratory Efficacy Endpoints

[redacted]

[redacted] In addition, two-sided 95% CI on mean change from baseline by visit will be calculated based on the paired t-test. P-value on change from baseline by visit will be provided based on the paired t-test.

The number and percentage of participants in each category for each item of CGPQ at Week 12 (Visit 8) for participants who receive 1 treatment session, or at Week 20 (Visit 9) for participants who receive 2 treatment sessions, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021 will be summarized for the Evaluable Population 1 and Evaluable Population 4.

The number and percentage of participants in each category of CSQ-Midsection Item 2 at Week 12 (Visit 8) for participants who receive 1 treatment session, or at Week 20 (Visit 9) for participants who receive 2 treatment sessions, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021 will be summarized for the Evaluable Population 1 and the two-sided Fisher's exact 95% CI on the percentage of participants with improvement (a lot of improvement, moderate improvement, and a little improvement) will be provided.

The number and percentage of participants reporting noticeable improvement in any treated body area, all treated body areas, and each treated body area at Week 4 (Visit 4) post treatment session 1 will be summarized for the Evaluable Population 1 (midsection) and Evaluable Population 2 (other treated body areas) and Evaluable Population 3 (any treated body area, all treated body areas) and the two-sided Fisher's exact 95% CI on the percentage will be provided.

For midsection, the descriptive statistics of the adjusted total volume of fat (cc) at baseline and post-baseline visits, [redacted]

For outer thigh (left, right, and combined left and right) and submental area, the descriptive statistics of the volume of fat (cc) change from baseline values will be provided for the Evaluable Population 2.

[redacted]

The number and percentage of participants with correct identification of baseline vs. 4-week post treatment session 1 by 2/3 and 3/3 blinded, independent reviewers for the following body areas will be summarized for the Evaluable Population 1 (midsection) and Evaluable Population 2 (other treated body areas) and the two-sided Fisher's exact 95% CI on the percentage will be provided:

- Midsection
- Upper arms
- Inner thighs
- Outer thighs
- Submental area

[redacted]

9.6 Effectiveness Subgroup Analyses

The following subgroup analyses for the primary and secondary effectiveness endpoints will be provided:

- Subgroup analysis for primary effectiveness endpoint:

- Response on CSQ-midsection item #1 (overall satisfaction) at 12-week follow-up of final treatment by number of treatment cycles completed
- Response on CSQ-midsection item #1 (overall satisfaction) at 12-week follow-up of final treatment by country

- Subgroup analysis for secondary effectiveness endpoints:
  - Response on CSQ item #1 (CSQ-overall and CSQ for individual treated body area) at 12-week follow-up of final treatment by number of treatment cycles completed
  - Response on CSQ item #1 (CSQ-overall and CSQ for individual treated body area) at 12-week follow-up of final treatment by country
  - Number and proportion of participants with correct identification of baseline vs 12-week post-final treatment images by number of treatment cycles completed
  - Number and proportion of participants with correct identification of baseline vs 12-week post final treatment images by country

- [redacted]

10.0 Safety Analyses

10.1 General Considerations

All safety analyses will be conducted in the Safety Population. Baseline is defined as the last non-missing assessment before the first Coolsculpting procedure.

10.2 Adverse Events

Adverse events (AEs) will be coded into SOC and PT using the MedDRA. The actual version of the MedDRA will be noted in the statistical tables and clinical study report.

An AE will be considered an adverse device effect (ADE) if the AE has a reasonable possibility (Possible, Probable, or Causal relationship) that the study device caused the event.

An AE will be considered a study procedure related AE if the AE has a reasonable possibility (Possible, Probable, or Causal relationship) that the study procedure caused the event.

If the causal relationship to the study procedure/device is missing, the AE will be considered as related to the study procedure/device. If the severity is missing, the AE will be considered as severe.

10.2.1 Treatment-Emergent Adverse Events

An AE (or ADE) will be considered a treatment-emergent adverse event (TEAE) (or treatment-emergent adverse device effect [TEADE]) if the AE (or ADE) began or worsened (increased in severity or became serious) on or after the date (and time, if known) of the first study intervention. An AE (or ADE) will be considered a treatment-emergent serious adverse event (TESAE) (or treatment-emergent serious adverse device effect [TESADE]) if it is a TEAE (or TEADE) that additionally meets any SAE (or SADE) criterion. Product label for CoolSculpting report and risk analysis report will be provided by Abbvie before database lock. Any AE (or ADE) not listed on either document will be considered as an unanticipated AE (or ADE).

TEAEs and TEADEs occurred on or after the date of treatment session 1 and before the date of treatment session 2 are counted for treatment session 1. TEAEs and TEADEs occurred on or after the date of treatment session 2 are counted for treatment session 2.

All AEs and ADEs will be included in data listings. Only TEAEs and TEADEs will be included for summaries, unless stated otherwise. Participants with TEAEs/TEADEs, TEAEs related to study procedure, TESAEs/TESADEs, unanticipated TEAEs/TEADEs (UTEAEs/UTEADEs), unanticipated TESAEs/TESADEs (UTESAEs/UTESADEs), TEAEs leading to discontinuation, and TEAEs leading to death will be summarized.

10.2.2 Adverse Event Overview

Overall summaries of TEAEs will include:

- The number and percentage of participants reporting at least one TEAE
- The number and percentage of participants reporting at least one TESAE
- The number and percentage of participants reporting at least one UTEAE
- The number and percentage of participants reporting at least one UTESAE
- The number and percentage of participants reporting at least one TEAE related to study procedure
- The number and percentage of participants reporting at least one TESAE related to study procedure
- The number and percentage of participants reporting at least one TEADE
- The number and percentage of participants reporting at least one TESADE
- The number and percentage of participants reporting at least one UTEADE
- The number and percentage of participants reporting at least one UTESADE
- The number and percentage of participants reporting a TEAE leading to study discontinuation
- The number and percentage of participants reporting a TEAE leading to death

10.2.3 Treatment-Emergent Adverse Events by SOC and/or PT

The number and percentage of participants will be summarized by SOC and PT, with or without by severity, as follows:

- TEAEs by SOC and PT
- TEAEs by SOC, PT, and severity
- Study Procedure Related TEAEs by SOC and PT

- Study Procedure Related TEAEs by SOC, PT and severity
- TEADEs by SOC and PT
- TEADEs by SOC, PT, and severity
- UTEAEs by SOC and PT
- UTESAEs by SOC and PT
- UTEADEs by SOC and PT
- UTESADEs by SOC and PT
- TESAEs by SOC and PT
- TESAEs by SOC, PT and severity
- Study Procedure Related TESAEs by SOC and PT
- Study Procedure Related TESAEs by SOC, PT and severity
- TESADEs by SOC and PT
- TESADEs by SOC, PT, and severity
- TEAEs leading to study discontinuation by SOC and PT
- TEAEs leading to death by SOC and PT

The AE and ADE summary tables will be presented with SOC in alphabetical order and in decreasing frequency within each SOC. If more than 1 AE or ADE is coded to the same PT for the same participant, the participant will be counted only once for that PT using the most severe and most related occurrence for the summarization by severity and by relationship to study intervention.

10.2.4 SAEs (Including Deaths) and Adverse Events Leading to Study Discontinuation

An SAE is defined as an AE that:

- led to death
- led to serious deterioration in the health of the participant, that either resulted in
    - a life-threatening illness or injury; or
    - a permanent impairment of a body structure or a body function, or
    - in-patient or prolonged hospitalization; or
    - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function;
    - Chronic disease (EU)
- Led to fetal distress, fetal death, or a congenital abnormality or birth defect

TESAEs, study procedure related TESAEs, TESADEs, TEAEs leading to study discontinuation, and TEAEs leading to death will be summarized in the overall table as in Section 10.2.2, and by SOC and PT as in Section 10.2.3.

10.2.5 Adverse Events of Special Interest

Not applicable.

10.3 Analysis of Laboratory Data

Pregnancy test (urine β-HCG) will be performed on Visit 1, Visit 2, and Visit 6. The pregnancy test results will be listed but not summarized.

10.4 Safety Subgroup Analyses

For TEAEs, the following subgroup analyses will be provided:

- Subgroup analysis by SOC and PT:
    - TEAEs by treated body areas, SOC and PT
- Subgroup analysis by SOC, PT and severity:
    - TEAEs by number of treated body areas, SOC, PT, and severity

10.5 Other Safety Analyses

10.5.1 Pain Assessment

On Visit 2 and Visit 6, participant's pain rating 10 minutes into the treatment cycle and the worst pain rating during the treatment cycle will be captured. Pain assessment will also be performed on Visit 3, Visit 4, Visit 5, Visit 7, Visit 8, and Visit 9. The number and percentage of participants who experienced pain level in the pain assessment using a standard scale of 0 (no pain) to 10 (the worst pain imaginable) will be summarized by individual treated body area, combined treated body areas as specified in Section 6.0, visit and timepoint.

A listing will be provided for the pain assessment.

10.5.2 Post-treatment Clinical Assessment – Epidermal, Dermal, or Subcutaneous Findings

Clinical assessment immediately post-treatment and before post-treatment massage will be summarized by scale (1=mild, 2=moderate and 3=severe) for the following types of finding by individual treated body area, combined treated body areas as specified in Section 6.0 and visit:

- Erythema
- Bruising
- Swelling
- Purpura
- Petechiae
- Tenderness
- Soreness
- Other

Additionally, similar summary will be provided by treatment session and overall.

10.5.3 Post-treatment Clinical Assessment – Alteration in Sensation

Post-treatment clinical assessment for alteration in sensation will be summarized by scale (1=mild, 2=moderate and 3=severe) for the following types of alteration in sensation by individual treated body area, combined treated body areas as specified in Section 6.0 and visit:

- Burning Sensation
- Numbness
- Tingling
- Other

Additionally, similar summary will be provided by treatment session and overall.

10.5.4 Medical Device Deficiencies

The numbers and percentage of participants with device deficiencies will be summarized by suspect medical device and CoolSculpting applicator type.

11.0 Other Analyses

Not applicable.

12.0 Interim Analyses

Not applicable.

13.0 Overall Type-I Error Control

Not applicable.

14.0 Version History

SAP Version History Summary

Version	Date	Summary
0.1	09 June 2021	First draft
0.2	21 June 2021	Second draft, updated based on comments from Abbvie
0.3	15 October 2021	Third draft, updated based on comments from Abbvie
0.4	04 March 2022	Fourth draft, updated based on comments from Abbvie
0.5	05 April 2022	Fifth draft, updated based on comments from Abbvie
0.6	08 April 2022	Final draft, updated based on comments from Abbvie
1.0	11 April 2022	Final version
1.1	21 July 2022	Updated final version, changes include: Updated the definitions of Evaluable Population 1, 2, 3 and 4 (Section 4.0). [redacted] Updated participant disposition, treatment exposure, demographic and baseline characteristics, and effectiveness analyses based on comments from Abbvie (Section 5.0 to Section 9.6).
2.0	29 July 2022	Updated final version

15.0 References

Not applicable.

Thighs and Submental Area) whether midsection treatment is completed or not, and do not have any significant protocol deviation or violation .

The Evaluable Population 3 will consist of all participants who completed the cryolipolysis treatment plan for any body areas (Midsection, Upper Arms, Inner Thighs, Outer Thighs and Submental Area) and do not have any significant protocol deviation or violation.

The Evaluable Population 4 will consist of all participants who completed the cryolipolysis treatment plan to the midsection and one or more additional body areas (Upper Arms, Inner Thighs, Outer Thighs and Submental Area) and do not have any significant protocol deviation or violation.

5.0 Participant Disposition

The number of participants who are in the Enrolled Population and the number and percentage of participants who are in the Safety Population, Evaluable Population 1, Evaluation Population 2, Evaluable Population 3, and Evaluable Population 4 will be summarized. Under Evaluable Population 2, the number and percentage of participants who completed each individual treated body area (Upper Arms, Inner Thighs, Outer Thighs and Submental Area) will be summarized. The number and percentage of screen failure participants and the screen failure reasons will also be summarized for the Enrolled Population.

The number and percentage of participants who complete the study and who prematurely discontinue from study will be presented for the Safety Population; furthermore, the number and percentage of participants discontinued prematurely from study will be presented for the Safety Population by the primary reason for discontinuation as collected on the eCRF. Reasons for premature discontinuation from the study include:

- Adverse Event
- Withdrawal of consent
- Pregnancy
- Protocol Deviation
- PI Discretion
- Chronic Disease (for EU only)

- Lost to follow-up
- Other

A Listing of participant disposition will be provided for the Enrolled Population.

6.0 Treatment Exposure and Compliance

The total number of completed treatment cycles will be summarized using descriptive statistics (n, mean, SD, median, Q1, Q3, minimum and maximum) for combined treated body areas, by each treatment session and overall for the Safety Population, Evaluable Population 1, Evaluable population 2, Evaluable Population 3, and Evaluable Population 4. Combined treated body areas including combined upper and lower abdomens, combined right and left flanks, combined upper and lower abdomens and right and left flanks, combined right and left upper arm, combined right and left inner thigh, combined right and left outer thigh, and all combined treated body areas. The average percentage of overlapping treatment on each body area will be listed but not summarized.

The number and percentage of treatments interrupted or discontinued along with the reason will be presented for individual treated body area, and for combined treated body areas as specified in Section 6.0, by treatment session and overall for the Safety Population.

The number and percentage of participants with single, dual, triple, or quad applicators used will be summarized by country, treatment session and overall for the Safety Population.

The completed treatment plan will be summarized by country, treatment round, treatment session and overall for the Safety Population.

The study investigators are responsible for performing the study in compliance with the protocol. The treatment compliance will not be applicable in the study.

All treatment exposure data will be listed for the Safety Population.

7.0 Demographics, Baseline Characteristics, Medical History, and Prior/Concomitant Medications

7.1 Demographics and Baseline Characteristics

Demographic parameters will be summarized descriptively for the Safety Population, Evaluable Population 1, and Evaluable Population 2. Demographic parameters include age, sex (if female, childbearing potential), race, and ethnicity, where race and ethnicity are collected only at sites in US and Singapore. Demographic parameters will also be summarized descriptively by treated body area for the Evaluable Population 3.

Baseline characteristics will be summarized descriptively for the Safety Population, Evaluable Population 1, and Evaluable Population 2. Baseline characteristics include weight, height, Fitzpatrick Skin Type (I, II, III, IV, V, VI), and body mass index (BMI). Baseline characteristics will also be summarized descriptively by treated body area for the Evaluable Population 3.

Demographic and baseline characteristics will be provided in a listing for the Safety Population.

7.2 Medical, Surgical and/or Cosmetic History

Medical, surgical and/or cosmetic procedural history data will be coded using the Medical Dictionary for Regulatory Activities (MedDRA). The actual version of the MedDRA will be noted in the statistical tables and clinical study report. The number and percentage of participants in each system organ class (SOC) and preferred term (PT) will be summarized for the Safety Population.

The summary table by SOC and PT will be presented with SOC in alphabetical order and PT in decreasing frequency within each SOC. If more than one medical history term is coded to the same PT for the same participant, the participant will be counted only once for that PT.

A listing will be provided for the Safety Population.

7.3 Prior and Concomitant Medications

A prior medication is defined as any medication that started and stopped prior to the date of the first CoolSculpting Elite procedure.

A concomitant medication is defined as any medication that started prior to the date of the first CoolSculpting Elite procedure and continued after the first CoolSculpting Elite procedure, or any medication that started on or after the date of first CoolSculpting Elite procedure.

Prior and concomitant medications will be coded using the World Health Organization Drug Dictionary (WHO DD). The actual version of the WHO DD will be noted in the statistical tables and clinical study report.

The number and percentage of participants with use of prior and concomitant medications will be summarized separately, by anatomic therapeutic chemistry (ATC) class and PT for the Safety Population. The summary will be presented with ATC class in alphabetical order and PT in decreasing frequency within each ATC class. If a participant took a specific medication multiple times or took multiple medications within a specific PT, that participant would be counted only once for the PT.

A listing will be provided for the Safety Population.

7.4 Concomitant Procedures

All concomitant procedures will be listed for the Safety Population.

7.5 Protocol Deviations and Violations

A protocol deviation (PD) is any non-adherence to study procedures that does not result in additional risk to the participant. Protocol deviations will be reviewed and documented before database lock.

A protocol violation (PV) is any non-adherence to the protocol that may result in significant additional risk to the participant (eg, enrollment of a participant who does not meet the study criteria). A protocol violation can also be an event of non-adherence to GCPs that may impact participant safety (eg, failure to obtain proper consent before performing study procedures). Violations should be reported to the study sponsor and the IRB within 5 working days if they occur.

Significant PDs/PVs (equivalent to major PDs/PVs as collected in data) listed below will be identified before database lock. The number and percentage of participants with significant PDs/PVs will be summarized for the Safety Population. Significant PDs/PVs related to the following categories which impact the study conduct, data validity or integrity for the study outcomes will be included:

- Key inclusion criteria

- Key exclusion criteria
- Withdrawal criteria
- Treatment
- Concomitant medications
- Timeframe deviation

A listing will be provided for the Enrolled Population.

8.0 Handling of Potential Intercurrent Events for the Primary and Key Secondary Endpoints

Not applicable.

9.0 Effectiveness Analyses

9.1 General Considerations

All effectiveness analyses will be conducted in the Evaluable Population 1, 2, 3 and 4. Baseline for effectiveness is defined as the last non-missing effectiveness assessment before the first Coolsculpting procedure. All Confidence Intervals (CIs) will be 2-sided 95% CIs, unless stated otherwise.

The summaries will be provided by participants with 1 treatment session, participants with 2 treatment sessions and overall, where applicable.

9.2 Handling of Missing Data

No imputation of missing data will be made for any effectiveness analysis.

9.3 Primary Effectiveness Endpoint(s) and Analyses

9.3.1 Primary Effectiveness Endpoint(s)

The primary effectiveness endpoint of this study is the proportion of participants with "satisfied" or "very satisfied" on the Item 1 for the CSQ-Midsection, measured at Week 12 (Visit 8) for participants who receive 1 treatment session, or at Week 20 (Visit 9) for participants who receive 2 treatment sessions, or at 12 weeks +14 days post treatment

session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021.

9.3.2 Main Analysis of Primary Effectiveness Endpoint(s)

The CSQ consists of 6 versions: CSQ-Midsection, CSQ-Overall, CSQ-Upper Arms, CSQ-Inner Thighs, CSQ-Outer Thighs, CSQ-Fat under chin. However, only CSQ-Midsection will be used for the primary analysis. In each version, the CSQ Item 1 is about rating the participant overall satisfaction with the results of the fat reduction procedure on the treated body area based on the following categories:

- Very satisfied
- Satisfied
- Neither satisfied nor dissatisfied
- Dissatisfied
- Very dissatisfied

The number and percentage of participants with "satisfied" or "very satisfied" on the Item 1 for the CSQ-Midsection at Week 12 (Visit 8) for participants who receive 1 treatment session, or at Week 20 (Visit 9) for participants who receive 2 treatment sessions, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021 will be summarized for the Evaluable Population 1 and the two-sided Fisher's exact 95% CI on the percentage will be provided.

A listing will be provided for CSQ-Midsection for the Safety Population.

9.3.3 Sensitivity and Supplementary Analyses of the Primary Effectiveness Endpoint(s)

Not applicable.

9.4 Secondary Effectiveness Endpoints and Analyses

9.4.1 Key Secondary Effectiveness Endpoints

The key secondary effectiveness endpoints include:

- The proportion of participants who received treatment to abdomen and flank and one or more additional body areas for treatment with "satisfied" or "very satisfied" on CSQ-Overall Item 1 measured at Week 12 (Visit 8, 12-week follow-up) for participants who receive only 1 treatment session to all treated body areas, or at Week 20 (Visit 9, 12-week follow-up) for participants who receive 2 treatment sessions to any or all treated body areas, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021.

- The proportion of participants with "satisfied" or "very satisfied" on individual treated body area (upper arms, inner thighs, outer thighs, fat under chin) CSQ Item 1 measured at Week 12 (Visit 8, 12-week follow-up) for participants who receive only 1 treatment session, or at Week 20 (Visit 9, 12-week follow-up) for participants who receive 2 treatment sessions for the respective treated body areas, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021.

- Correct identification of baseline vs 12-week post-final treatment images of the treated body area(s) by at least two out of three blinded, independent reviewers for the following body areas:

    - Midsection
    - Upper arms
    - Inner thighs
    - Outer thighs
    - Submental area

  Success will be defined as at least 70% correct identification of the pre-treatment images.

9.4.2 Main Analyses of Key Secondary Effectiveness Endpoints

The number and percentage of participants with "satisfied" or "very satisfied" on the Item 1 for the CSQ-Overall, CSQ-Upper Arms, CSQ-Inner Thighs, CSQ-Outer Thighs and CSQ-Fat Under Chin, at Week 12 (Visit 8) for participants who receive 1 treatment session, or at Week 20 (Visit 9) for participants who receive 2 treatment sessions, or at 12 weeks +14 days post treatment session 2 for participants who had their treatment session 2 rescheduled because of the CoolSculpting® Elite treatment hold in the US on / after 24th August 2021 will be summarized for the Evaluable Population 4 (overall) and Evaluable

10.2 Adverse Events

Adverse events (AEs) will be coded into SOC and PT using the MedDRA. The actual version of the MedDRA will be noted in the statistical tables and clinical study report.

An AE will be considered an adverse device effect (ADE) if the AE has a reasonable possibility (Possible, Probable, or Causal relationship) that the study device caused the event.

An AE will be considered a study procedure related AE if the AE has a reasonable possibility (Possible, Probable, or Causal relationship) that the study procedure caused the event.

If the causal relationship to the study procedure/device is missing, the AE will be considered as related to the study procedure/device. If the severity is missing, the AE will be considered as severe.

10.2.1 Treatment-Emergent Adverse Events

An AE (or ADE) will be considered a treatment-emergent adverse event (TEAE) (or treatment-emergent adverse device effect [TEADE]) if the AE (or ADE) began or worsened (increased in severity or became serious) on or after the date (and time, if known) of the first study intervention. An AE (or ADE) will be considered a treatment-emergent serious adverse event (TESAE) (or treatment-emergent serious adverse device effect [TESADE]) if it is a TEAE (or TEADE) that additionally meets any SAE (or SADE) criterion. Product label for CoolSculpting report and risk analysis report will be provided by Abbvie before database lock. Any AE (or ADE) not listed on either document will be considered as an unanticipated AE (or ADE).

TEAEs and TEADEs occurred on or after the date of treatment session 1 and before the date of treatment session 2 are counted for treatment session 1. TEAEs and TEADEs occurred on or after the date of treatment session 2 are counted for treatment session 2.

All AEs and ADEs will be included in data listings. Only TEAEs and TEADEs will be included for summaries, unless stated otherwise. Participants with TEAEs/TEADEs, TEAEs related to study procedure, TESAEs/TESADEs, unanticipated TEAEs/TEADEs (UTEAEs/UTEADEs), unanticipated TESAEs/TESADEs (UTESAEs/UTESADEs), TEAEs leading to discontinuation, and TEAEs leading to death will be summarized.

10.2.2 Adverse Event Overview

Overall summaries of TEAEs will include:

- The number and percentage of participants reporting at least one TEAE
- The number and percentage of participants reporting at least one TESAE
- The number and percentage of participants reporting at least one UTEAE
- The number and percentage of participants reporting at least one UTESAE
- The number and percentage of participants reporting at least one TEAE related to study procedure
- The number and percentage of participants reporting at least one TESAE related to study procedure
- The number and percentage of participants reporting at least one TEADE
- The number and percentage of participants reporting at least one TESADE
- The number and percentage of participants reporting at least one UTEADE
- The number and percentage of participants reporting at least one UTESADE
- The number and percentage of participants reporting a TEAE leading to study discontinuation
- The number and percentage of participants reporting a TEAE leading to death

10.2.3 Treatment-Emergent Adverse Events by SOC and/or PT

The number and percentage of participants will be summarized by SOC and PT, with or without by severity, as follows:

- TEAEs by SOC and PT
- TEAEs by SOC, PT, and severity
- Study Procedure Related TEAEs by SOC and PT

- Study Procedure Related TEAEs by SOC, PT and severity
- TEADEs by SOC and PT
- TEADEs by SOC, PT, and severity
- UTEAEs by SOC and PT
- UTESAEs by SOC and PT
- UTEADEs by SOC and PT
- UTESADEs by SOC and PT
- TESAEs by SOC and PT
- TESAEs by SOC, PT and severity
- Study Procedure Related TESAEs by SOC and PT
- Study Procedure Related TESAEs by SOC, PT and severity
- TESADEs by SOC and PT
- TESADEs by SOC, PT, and severity
- TEAEs leading to study discontinuation by SOC and PT
- TEAEs leading to death by SOC and PT

The AE and ADE summary tables will be presented with SOC in alphabetical order and in decreasing frequency within each SOC. If more than 1 AE or ADE is coded to the same PT for the same participant, the participant will be counted only once for that PT using the most severe and most related occurrence for the summarization by severity and by relationship to study intervention.

10.2.4 SAEs (Including Deaths) and Adverse Events Leading to Study Discontinuation

An SAE is defined as an AE that:

- led to death
- led to serious deterioration in the health of the participant, that either resulted in
    - a life-threatening illness or injury; or
    - a permanent impairment of a body structure or a body function, or
    - in-patient or prolonged hospitalization; or
    - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function;
    - Chronic disease (EU)
- Led to fetal distress, fetal death, or a congenital abnormality or birth defect

TESAEs, study procedure related TESAEs, TESADEs, TEAEs leading to study discontinuation, and TEAEs leading to death will be summarized in the overall table as in Section 10.2.2, and by SOC and PT as in Section 10.2.3.

10.2.5 Adverse Events of Special Interest

Not applicable.

10.3 Analysis of Laboratory Data

Pregnancy test (urine β-HCG) will be performed on Visit 1, Visit 2, and Visit 6. The pregnancy test results will be listed but not summarized.

10.4 Safety Subgroup Analyses

For TEAEs, the following subgroup analyses will be provided:

- Subgroup analysis by SOC and PT:
    - TEAEs by treated body areas, SOC and PT
- Subgroup analysis by SOC, PT and severity:
    - TEAEs by number of treated body areas, SOC, PT, and severity

10.5 Other Safety Analyses

10.5.1 Pain Assessment

On Visit 2 and Visit 6, participant's pain rating 10 minutes into the treatment cycle and the worst pain rating during the treatment cycle will be captured. Pain assessment will also be performed on Visit 3, Visit 4, Visit 5, Visit 7, Visit 8, and Visit 9. The number and percentage of participants who experienced pain level in the pain assessment using a standard scale of 0 (no pain) to 10 (the worst pain imaginable) will be summarized by individual treated body area, combined treated body areas as specified in Section 6.0, visit and timepoint.

A listing will be provided for the pain assessment.

10.5.2 Post-treatment Clinical Assessment – Epidermal, Dermal, or Subcutaneous Findings

Clinical assessment immediately post-treatment and before post-treatment massage will be summarized by scale (1=mild, 2=moderate and 3=severe) for the following types of finding by individual treated body area, combined treated body areas as specified in Section 6.0 and visit:

- Erythema
- Bruising
- Swelling
- Purpura
- Petechiae
- Tenderness
- Soreness
- Other

Additionally, similar summary will be provided by treatment session and overall.

10.5.3 Post-treatment Clinical Assessment – Alteration in Sensation

Post-treatment clinical assessment for alteration in sensation will be summarized by scale (1=mild, 2=moderate and 3=severe) for the following types of alteration in sensation by individual treated body area, combined treated body areas as specified in Section 6.0 and visit:

- Burning Sensation
- Numbness
- Tingling
- Other

Additionally, similar summary will be provided by treatment session and overall.

10.5.4 Medical Device Deficiencies

The numbers and percentage of participants with device deficiencies will be summarized by suspect medical device and CoolSculpting applicator type.

11.0 Other Analyses

Not applicable.

12.0 Interim Analyses

Not applicable.

13.0 Overall Type-I Error Control

Not applicable.