GALDERMA

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Galderma

Protocol Name: Study comparing **T**reatment with **A**lluzience vs **R**econstituted toxin **(*STAR)***

Clinical Trial Number (CTN): 05PF2005

A Phase IV, Randomized, Interventional, Study to Assess Subject Treatment Session Perception and Investigator Treatment Experience of Alluzience and Vacuum-Dried Botulinum Neurotoxin Type A for Aesthetic Use

Statistical Analysis Plan

CCI [redacted]

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1.0 PURPOSE

This statistical analysis plan (SAP) describes the methods to be used in the analysis of study data from Galderma STAR Protocol in order to answer the study objectives, and is based on version 5.0 of the study protocol, dated December 1, 2021, and version 1.0 of the electronic case report forms (eCRF), dated January 27, 2022.

Populations for analysis, data handling rules, statistical methods, and formats for data presentation are described within this document. The statistical analyses and summary tabulations described in this SAP will provide the basis for the results sections of the clinical study report (CSR) for this study. The SAP outlines any differences in data analysis methods relative to those planned in the study protocol.

2.0 ABBREVIATIONS

Below is the list of abbreviations that will be used throughout this document.

Abbreviation	Definition
AC	Advanced Clinical
AE	Adverse Event
ATC	Anatomical Therapeutic Chemical
BMI	Body Mass Index
BoNT-A	Botulinum Neurotoxin Type A
CDISC	Clinical Data Interchange Standards Consortium
CSP	Clinical Study Protocol
CSR	Clinical Study Report
eCRF	Electronic Case Report Form
eCTD	Electronic Common Technical Document
FAS	Full Analysis Set
GAIS	Global Aesthetic Improvement Scale
GL	Glabellar Lines
ICH	International Council for Harmonization
Max	Maximum
MedDRA	Medical Dictionary for Regulatory Activities
Min	Minimum
N	Number of Observations

Abbreviation	Definition
OC	Observed Case
PD	Protocol Deviation
PP	Per-Protocol
PT	Preferred Term
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
WHO	World Health Organization

3.0 OVERALL STUDY DESIGN AND OBJECTIVE

3.1 Study Objectives

3.1.1 Primary Study Objective

The primary objective of this study is to evaluate the time needed to prepare Alluzience and powder Botulinum Neurotoxin Type A (BoNT-A) according to protocol.

3.1.2 Secondary Study Objectives

The secondary objectives of the study are:

1. To evaluate preparation/reconstitution experience of Alluzience and powder BoNT-A.
2. To describe Investigator treatment experience when using Alluzience for the treatment of Glabellar Lines (GL).

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3.1.4 Safety Study Objective

The safety objective is to evaluate the safety of a single dose of Alluzience for the treatment of moderate to severe GL.

3.2 Study Design

This is an open-label, randomized, interventional, two-armed, multi-centre study to investigate subject treatment perception and Investigator treatment experience when using Alluzience or vacuum-dried BoNT-A (powder BoNT-A) for treatment of GL. Subjects randomized to be treated with powder BoNT-A will only be followed for 1 month (Visit 3) while subjects treated with Alluzience will be followed for 6 months (Visit 6).

3.3 Treatments and Assignment to Treatments

As a screen failure rate of approximately 10% is anticipated, approximately 170 subjects will be screened. Approximately 150 subjects will be randomized to either Alluzience or powder BoNT-A treatment in a CCI ratio. Randomization will be stratified by study site.

3.4 Determination of Sample Size

The sample size of approximately 150 subjects, 100 subjects in the Alluzience treatment group and 50 in the powder BoNT-A treatment group, is not based on a statistical calculation. The selected number of subjects is regarded as sufficient for an evaluation of the studied endpoints by using descriptive statistics.

4.0 GENERAL ANALYSIS CONVENTION

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4.1 Trial Periods

4.1.1 Alluzience Group

The study consists of six visits for the Alluzience group: screening (Visit 1), treatment (Baseline/Visit 2) and four follow-up visits at 1 (Visit 3), 3 (Visit 4), 5 (Visit 5) and 6 (Visit 6) months after treatment. The screening visit and the treatment visit might be conducted at the same day.

4.1.2 Powder BoNT-A Group

The study consists of three visits for the powder BoNT-A group: screening (Visit 1), treatment (Baseline/Visit 2) and a follow-up visit at Month 1 (Visit 3). The screening visit and the treatment visit might be conducted at the same day.

4.2 Visit Windows

Study visits are expected to occur according to the protocol schedule (Appendix A). When necessary, unscheduled visits may be conducted, in particular if an AE occurs and needs to be assessed and/or treated. Questionnaire scores for unscheduled visits will only be included in data listings. All data will be tabulated per the evaluation visit as recorded on the eCRF. In data listings, the relative study day of all dates will be presented.

If date of assessment >= date of first dose of study drug:
Relative Study Day = [date of assessment – date of first dose of study drug] + 1

If date of assessment < date of first dose of study drug:
Relative Study Day = date of assessment – date of first dose of study drug

5.0 ANALYSIS POPULATIONS

5.1 Full Analysis Set (FAS) Efficacy Population

The FAS includes all randomized and treated subjects. FAS will be used for all efficacy evaluations.

5.2 Per-Protocol (PP) Efficacy Population

The Per Protocol (PP) population is a subset of the subjects in the FAS population who complete the Month 1 visit and have no protocol deviations (PD) considered to have a substantial impact on the primary efficacy outcome. The primary efficacy endpoint will be evaluated using the PP population if the PP population consists of less than 95% of the FAS population.

5.3 Safety Population

The safety population includes all subjects who were administered study product (i.e., Alluzience or powder BoNT-A). Safety analysis will be performed based on the Safety population.

6.0 SUBJECT DISPOSITION

Overall subject disposition will include the number of subjects screened, the number of subjects randomized to each treatment arm, the number of subjects in each analysis population (safety, FAS, and PP populations), and the number of subjects who withdrew from the study and the reasons for withdrawal.
Subject disposition by visit will show the number of subjects who completed each visit for the FAS population. Listings of screen failures (including inclusion/exclusion criteria) will be also presented.

7.0 DEMOGRAPHIC AND BASELINE CHARACTERISTICS

The FAS population will be used to summarize the data under this section. The summary will be done with appropriate descriptive statistics. Specifically, number and percentages will be provided for categorical variables, and mean, SD, median, min/max for continuous variables. All tables will be presented by treatment arm and overall.

7.1 Demographic Characteristics

Demographic characteristics at study entry will be summarized by treatment and overall. No formal statistical comparisons between treatment groups will be performed. Tables and listings will be presented.

Demographic variables to be summarized are:

- Age (years)
- Sex
- Child-bearing potential, for females only
- Race
- Ethnicity
- Age category (<30 years, 31-64 years and ≤ median age, > median age)
- Weight (kg)
- Body mass index (BMI) (kg/m^2)
- Height (cm)
- Subject is toxin naïve or non-toxin naïve

7.2 Cosmetic/Aesthetic Procedures and Implant History

Cosmetic/Aesthetic procedures and implant history will be summarized by treatment in a table and reported by treatment and subject in a data listing. The table will be sorted by overall incidence first and then alphabetically. The listing will show the verbatim term (i.e., term reported by the site), as well as the Medical Dictionary for Regulatory Activities (MedDRA) version 24.1 or later System Organ Class (SOC) and Preferred Term (PT) associated with the verbatim term. The listing will include the procedure/product name, procedure/product location and date of procedure.

7.3 Medical History

Medical history information will be summarized by treatment in a table and reported by treatment and subject in a data listing. The table will be sorted by overall incidence first and then alphabetically. The listing will show the verbatim term (i.e., term reported by the site), as well as the Medical Dictionary for Regulatory Activities (MedDRA) version 24.1 or later System Organ Class (SOC) and Preferred Term (PT) associated with the verbatim term. Start and end dates (or ongoing at the time of consent) will also be included in the listing.

7.4 Concomitant Procedures

Medical and surgical procedures, including, but not limited to, laser/radiation procedures, dermal fillers (area of treatment should be indicated), X-rays, surgeries, other facial procedures, and tooth extractions will be summarized by treatment in a table and reported by treatment and subject in a data listing. The table will be sorted by overall incidence first and then alphabetically. The listing will show the verbatim term (i.e., term reported by the site), as well as the Medical Dictionary for Regulatory Activities (MedDRA) version 24.1 or later System Organ Class (SOC) and Preferred Term (PT) associated with the verbatim term. Start and end dates (or ongoing at the time of consent) will also be included in the listing.

7.5 Protocol Deviations

Protocol Deviations (PDs) are defined as a divergence or departure from the clinical trial design or procedures as described in the approved trial protocol and protocol amendments. A Grade 1 PD is defined as a breach which does or will affect the safety and/or rights of a trial subject or the reliability and robustness of data generated in the clinical trial or the scientific value of the trial. A Grade 2 PD is defined as a breach which might affect the safety and/or rights of a trial subject or the reliability and robustness of data generated in the clinical trial or the scientific value of the trial. A Grade 3 PD is defined as a breach/deviation which does not affect the safety or rights of a trial subject or the reliability or robustness of the trial data or affect the scientific value of the trial.

For this study, the protocol deviations are identified (but not limited to) in Table 1 below. Protocol violators resulting in exclusion from the PP population will be identified by the sponsor and documented prior to the database freeze.

Table 1: Protocol deviations

Deviation Type
SAE Reporting
Study Product Use
Missed Procedure
Eligibility
Photography
Informed Consent
Missed Visit
Prohibited medication or procedure
Out of Window visit
Remote visit all assessments done
Remote visit all assessments not done, specify

The number and percentage of subjects with a PD and the type of PD will be summarized for the FAS population by site, treatment arm and overall. Percentages will be based on the total FAS population. A listing of PDs will be provided.

7.5.1 Out of Window visit duration

When a subject performs a planned study visit outside of the protocol-specified visit windows (Appendix A), the subject has an out of window study visit, which is considered a type of protocol deviation for this study. Knowing a subject's Screening visit (Visit 1) and Baseline visit (Visit 2) and using the protocol-specified visit windowing, one can calculate a subject's target study visit window date range for each planned study visit. Then, by comparing a subject's actual study visit date to the target study visit window date range, one can calculate the days over/under the actual study visit was in relation to the target study visit date, or study visit out of window duration.

The duration, in days, a study visit is out of window will be summarized by treatment group, overall, and by visit. Out of window visit durations will also be presented by site as well. Duration will be split into the following below categories. Duration categories will include both days before and days after the target planned visit date.

- +/- 1-2 days
- +/- 3-7 days
- +/- 8-20 days

- +/- 21 or more days

The number and percentage of subjects within each out of window duration category will be presented descriptively. For the overall analysis, percentages will be calculated using the number of subjects with an out of window visit at the respective visit as the denominator; for the by site analysis, percentages will be calculated using the number of subjects at the respective site as the denominator.

8.0 CLINICAL QUESTIONNAIRES

8.1 Alluzience Preparation Questionnaire

The Alluzience Preparation Questionnaire (Appendix B) consists of 4 questions including the time for study product to equilibrate to room temperature and the time it took to prepare the product to have it ready for injection. The questionnaire will only be given on Visit 2.

8.2 BOTOX/Vistabel Reconstitution Questionnaire

The BOTOX/Vistabel Reconstitution Questionnaire (Appendix C) consists of 5 questions including the time for the solvent to equilibrate to room temperature and the time it took to prepare the product to have it ready for injection. The questionnaire will only be given on Visit 2.

8.3 Investigator Treatment Session Questionnaire (for Alluzience only)

The Investigator Treatment Session Questionnaire (Appendix D) should be completed by the Treating Investigator after the subject has been treated at Visit 2 (baseline). The Investigator Treatment Session Questionnaire consists of 12 questions, where each question has 5 possible values ranging from Strongly disagree to Strongly agree.

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9.0 EFFICACY VARIABLES

9.1 Primary Efficacy Variables

To address the primary endpoint of evaluating the time needed to prepare Alluzience and powder BoNT-A according to protocol, the time (in minutes) needed to prepare Alluzience will be calculated as:

- Alluzience: The sum of the "Time for study product to equilibrate to room temperature" and the answer to the question "How long did it take to prepare the product to have it ready for injection?" on the Alluzience Reconstitution Questionnaire.

- Powder BoNT-A: The sum of the "Time for solvent to equilibrate to room temperature" and the answer to the question "How long did it take to prepare the product to have it ready for injection?" on the BOTOX/Vistabel Reconstitution Questionnaire.

9.2 Secondary Efficacy Variables

Secondary efficacy variables to support secondary endpoints include:

9.2.1 Proportion of study products prepared by the investigators in front of the subjects

For the Alluzience treatment group, calculated as (number of subjects where the product was prepared in front of them / total number of subjects injected with Alluzience).

For the powder BoNT-A treatment group, calculated as (number of subjects where the product was reconstituted in front of them / total number of subjects injected with powder BoNT-A).

9.2.2 Proportion of technical issues/problems

Calculated as (number of subjects in response category X / total number of subjects injected with Alluzience), where response category X refers to the answer to whether the Investigator experienced any technical issues/problems when using a ready to use product as compared to a product to be reconstituted (strongly agree/agree/neither agree nor disagree/ disagree/ strongly disagree). This will be calculated for the Alluzience treatment group only.

9.2.3 Proportion of powder BoNT-A reconstitution issues

Calculated as (number of subjects with a product problem associated with the reconstitution / total number of subjects injected with powder BoNT-A). This will be calculated for the powder BoNT-A treatment group only.

Calculated as (number of times an investigator experienced any issues to reconstitute the powder BoNT-A in the past / total number of subjects injected with powder BoNT-A). This will be calculated for the powder BoNT-A treatment group only.

9.2.4 Investigator Treatment Session Questionnaire

The proportion of subjects in each answer will be calculated as (number of subjects in response category X / total number of subjects injected with same treatment). The Investigator Treatment Session Questionnaire (Alluzience only) at baseline will be analyzed.

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10.0 EFFICACY ANALYSIS

All proportions will be calculated using the FAS population for questions with an answer. The number of missing assessments will be included, but not part of the calculation. All efficacy analyses will be conducted using the FAS population, unless specified below.

10.1 Primary Efficacy Analysis

The primary endpoint is the time (in minutes) needed to prepare Alluzience and powder BoNT-A according to protocol. CCI [redacted]

10.1.1 Sensitivity Analysis

The primary efficacy analysis will be repeated on the Per-Protocol population.

10.2 Secondary Efficacy Analysis

All secondary endpoints will be analyzed by treatment group using n and percentages for each proportion. The proportion of answers to each question will be presented by visit and treatment.

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CCI [redacted]

CCI [redacted]

11.0 STATISTICAL/ANALYTICAL ISSUES

11.1 Handling of Dropouts or Missing Data

The number of missing values will be summarized and reported as appropriate. Missing values in the primary efficacy analysis will not be imputed. Sensitivity analyses using imputed data will be performed on statistical tests included in the secondary efficacy analyses (described in Section 10.2.9).

11.2 Multiple Comparisons/Multiplicity

No adjustments for multiple comparisons or multiplicity will be made.

CCI [redacted]

11.4 Interim Analysis and Data Monitoring

No interim analysis will be performed.

12.0 SAFETY ANALYSIS

All safety data will be summarized descriptively based on the safety population. All of the safety analyses will be done using Observed Case (OC).

12.1 Glabellar Lines Treatment Administration

The Glabellar Lines Treatment Administration will be presented in a table and in a data listing. The listing will include the treatment date, investigator ID, needle size, if the injection was performed according to the protocol and a description of the treatment procedure if the injection was not performed according to the protocol. Product complaints will also be presented in a data listing.

12.2 Adverse Events

According to ICH E2A, an adverse event (AE) is any untoward medical occurrence in a patient or a clinical investigation subject administered a pharmaceutical product, and which does not necessarily have a causal relationship with this treatment. An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product.

Thus, any new sign, symptom or disease, or any clinically significant worsening of an existing sign, symptom or disease (including new episodes of a chronic disease [e.g., hay fever, allergy]) compared to the condition at the first visit, should be considered an AE.

Adverse events will be summarized by treatment group using the safety population. All AEs will be coded using MedDRA version 24.1 or later and presented by MedDRA SOC and PT in alphabetic order for SOC and by descending number in the SOC group and alphabetic order if the percentages are equal for PTs within an SOC. An AE with an onset date on or after the start of dosing in the active treatment period will be considered a treatment-emergent adverse event (TEAE).

While every effort will be made to obtain complete information on every reported AE, the following imputation rules will be followed for any respective missing AE data:

CCI [redacted]

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12.2.1 Overview of Adverse Events

An overview summary table of AEs will be presented by treatment including the number and percentage of subjects reporting an AE for the following categories:

- Subjects reporting at least one AE
- Subjects reporting at least one treatment-related AE
- Subjects reporting at least one serious AE (SAE)
- Subjects reporting at least one treatment-related serious AE (SAE)
- Subjects reporting at least one AE leading to discontinuation of study
- Subjects with AE resulting in death on study

12.2.2 Overview of Treatment-Emergent Adverse Events

A TEAE is an event that emerges during or after treatment, having been absent pre-treatment, or worsens relative to the pre-treatment state.

The number of events and the number and percentage of subjects by treatment with the following categories of TEAEs will be summarized by SOC and PT:

- Subjects reporting at least one TEAE by SOC and PT.
- Subjects reporting at least one TEAE by SOC, PT, and maximum intensity.
- Subjects reporting at least one TEAE by SOC, PT, and relationship (related/not related) to study drug.
- Subjects reporting at least one TEAE leading to discontinuation of study drug dosing by SOC and PT.
- Subjects reporting at least one serious TEAE by SOC and PT.

The number and percentage of subjects who experienced at least one TEAE will be summarized overall and for each SOC and each PT. The percentage will be based on the number of subjects in the safety population. Each subject will contribute at most one count per summarization category. In other words, if a

subject has more than one TEAE with same PT, the subject will be counted only once for that PT. Similarly, if a subject has more than one TEAE for a SOC, the subject will be counted only once in that SOC and PT.

12.2.3 Relationship to Study Drug

A two-point scale (Yes/No) shall be used for the causality assessment. The Investigator shall be asked to indicate a response to each of the following questions in the eCRF:

- "Do you consider that there is a reasonable possibility that the event may have been caused by the study product?"
- "Do you consider that there is a reasonable possibility that the event may have been caused by the study product injection procedure?"

If the answer is "Yes" to either of these questions, the AE is considered related.

Summaries of related AEs (including the total number of events, number and percentage of subjects) will be displayed by treatment group according to the following:

- All AEs related to study product or injection procedure by SOC, PT, and maximum intensity (mild, moderate, or severe)
- All AEs related to study product or injection procedure by SOC, PT, and duration of event
- All AEs related to study product or injection procedure by SOC, PT, and number of days to onset of event
- All AEs by SOC, PT, and action taken (none, medical treatment, non-pharmacological treatment, subject withdrawn)
- All AEs unrelated to study product or injection procedure by SOC, PT, and maximum intensity (mild, moderate, or severe)

If a subject has multiple occurrences of the same SOC or PT, then only the related event will be summarized in the tables for that SOC and PT. Missing relationships will be considered related.

12.2.4 Intensity of the Adverse Event

TEAEs will be summarized by intensity. The intensity of the TEAE is classified into three categories of Mild, Moderate, and Severe. If a subject has multiple occurrences of the same SOC or PT with varying levels of intensity, then the subject will only be counted under the most severe intensity in the table. If the intensity assessment is missing, then an intensity of Severe will be assumed.

12.2.5 Death, Serious Adverse Events, Adverse Events Leading to Discontinuation

A Serious Adverse Event (SAE) is any untoward medical occurrence that

- Results in death,
- Is life threatening,
- Requires in-patient hospitalization or prolongation of existing hospitalization,
- Results in persistent or significant disability/incapacity
- Is a congenital anomaly/birth defect, or
- Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the safety of the subject, and may require medical or surgical intervention to prevent one of the outcomes listed in this definition. Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasia, or convulsions that do not result in hospitalization.

Table summaries and by-subject listings also will be provided for the following: subject deaths, SAEs, and adverse events leading to study discontinuation.

12.3 Prior and Concomitant Medications and Therapies

Previous therapies are defined as therapies that have been stopped within 4 weeks preceding the screening visit or within timeframes specified in the inclusion/exclusion criteria.

Concomitant therapies are defined as follows:

- Any existing therapies ongoing at the time of the screening visit.
- Any changes to existing therapies (such as changes in dose or formulation) during the course of the clinical study.
- Any new therapies received by the subject since the screening visit.

Drugs, including, but not limited to, prescription, over the counter, birth control pills/patches/hormonal devices, vitamins, herbal medicines/supplements, and homeopathic preparations are to be considered for previous and concomitant therapies

Medications will be included in the concomitant medication summary if they were taken on or after the date of the study drug administration, regardless of when the medication started.

Partial start dates for medications will be imputed via the following rules:

- Start Date
  - If start date is completely missing, it will be assumed that the medication started at baseline.
  - If the start date is missing the day, the baseline day will be used provided the imputed date is on or after the subject's randomization date; otherwise, the day of randomization will be used.
  - If the start date is missing the month, the randomization month will be used.
  - If the start date is missing the year, the baseline year will be used provided the imputed date is on or after the subject's randomization date; otherwise, the subsequent year after randomization will be used.
- End Date
  - If end date is completely missing, it will be assumed that the medication is still being taken and will not be imputed.
  - If the end date is missing the day, the last of the month will be used (i.e. UNK-JAN-2022 becomes 31-JAN-2022)
  - If the end date is missing the month, the subsequent month after the start date will be used.If the end date is missing the year, the year of randomization will be used (i.e. 01-JAN-UNK becomes 01-JAN-2022), provided the imputed date is after the start date; otherwise, the subsequent year after start date will be used.

Medications other than study drug will be summarized by the World Health Organization (WHO) Drug Dictionary Anatomical Therapeutic Chemical 3rd level (ATC-3) and preferred name for the FAS population. If the 3rd level term is not available, the next available level (e.g., ATC-2) will be used.

The number and percentage of the subjects who took each medication will be tabulated by treatment, the ATC-3 level and preferred name for concomitant medications. ATC-3 and preferred name will be presented in descending frequency

first, and then alphabetically if there are ties. Each subject will contribute at most one count per summarization category. All concomitant medication data for each subject will be included in the listings. Similar number and percentage of subjects who had concomitant therapies will be tabulated for FAS population by treatment arm. Prior and concomitant medications and therapies will be included in data listings.

12.4 Pregnancy Test

Urine pregnancy tests will be summarized in data listings.

13.0 QUALITY CONTROL

All data displays and analyses will adhere to the ICH Harmonized Tripartite Guideline: Structure and Content of Clinical Study Reports (ICH Topic E3).

All analyses will be performed using CCI [redacted]. Advanced Clinical will follow its standard operating procedures in the creation and quality control of all tables, listings, figures, and analyses.

The sponsor will review all tables, listings, and figures prior to final database lock. Final SAS datasets, programs and outputs will be transferred to the sponsor at project completion.

14.0 TABLES AND LISTING CONVENTIONS

Mock-ups for statistical tables and listings will accompany this SAP. Final formats for the statistical tables and listings may deviate from these mock-ups upon agreement with Sponsor. Footnotes will be used as needed to clarify the information that is presented in the tables and listings. Unless otherwise requested by Sponsor, the term 'subject' will be used in all tables and listings, in accordance with Clinical Data Interchange Standards Consortium (CDISC) standards.

All tables and listings will use landscape orientation. Margins will be at least 2.0 cm at the top and bottom and at least 0.8 cm on the left and right, excluding headers and footers, in accordance with electronic Common Technical Document (eCTD) guidelines. Font will be Courier New, unless otherwise specified, with an 8-point font size in most cases. Page numbering will be sequential within each table, listing, and figure. Column headers should be in initial capital letters. Units for numeric data will be included when appropriate.

Tables and data listings will be created from different SAS programs. A single program may produce multiple tables or multiple data listings from the same dataset (e.g., all clinical chemistry data listings may be generated by a single program).

14.1 Statistical Table Conventions

Mock-ups for statistical tables will include headers, title numbers, titles, column headers and footers, and a proposed layout for the display of data.

14.2 Data Listing Conventions

Mock-ups for data listings will include headers, title numbers, titles, column headers, and footers. Data listings will provide all data collected on the corresponding eCRF page or provided by external vendors, unless otherwise indicated. If there are too many fields to be fit into a single page, data should be grouped logically and the listings will be generated as Part I, Part II, etc.

In general, data listings should include all subjects with data. However, if only subjects who meet a certain condition are listed (e.g., subjects with SAEs) and no subjects meet the condition, the data listing will so indicate.

The sort order for data presented in data listings will be treatment arm and Subject ID, unless otherwise requested by Sponsor. Within a subject, data will be listed in chronological order. Whenever possible, formatted values will be displayed (i.e., decoded). Where applicable, calendar date and study day of evaluations/events will be provided in the data listings.

15.0 RECORD RETENTION

Records related to the activities listed in this plan will be retained according to AC SOP AD-005.

16.0 CHANGE HISTORY

Table 2 Changes in Analysis Planned in the Protocol

CSP Section	SAP section	Description/Rationale of Change
9.1.1.4	10.2.9	CCI [redacted]
9.1.2.1	11.3	
9.1.4	10.0	

17.0 APPENDICES

Appendix A: Table 1 - Schedule of Assessments
Appendix B: Alluzience Preparation Questionnaire
Appendix C: BOTOX/Vistabel Reconstitution Questionnaire
Appendix D: Investigator Treatment Session Questionnaire (for Alluzience only)
CCI [redacted]

18.0 SIGNATURE PAGE

Prepared By:

Name	Role	Signature
PPD	Biostatistician	PPD

Approved By: *The signature of the document approver means that the approver has read, understood and approved this document.*

Name	Role	Signature
PPD	Galderma PPD /Sr Clinical Data Analyst	PPD

Document is considered final upon date of last signature.

Appendix A: Table 1 – Schedule of Assessments

1 month = 4 weeks/28 days Visit windows are calculated from Baseline/Visit 2 if not otherwise specified.	**Visit 1** Group 1 and 2 Screening [1]	**Visit 2** Group 1 and 2 Treatment / Baseline[1] (within 3 weeks after screening)	**Visit 3/** Group 1 EoS Group 2 1-Month Follow-up (±7 days)	**Visit 4** Group 1 3-Month Follow-up (±7 days)	**Visit 5** Group 1 5-Month Follow-up (±7 days)	**Visit 6/ET** EoS Group 1 6-Month Follow-up (±7 days)
Informed Consent	X	(X)[2]				
Demographic Data including, medical history & con-current diseases, previous facial treatments/ procedures	X	(X)[2]				
Inclusion /Exclusion Criteria	X	X				
Adverse Events[3]		X	X	X	X	X
Concomitant Medication/ Procedures	X	X	X	X	X	X
Urine Pregnancy Test[4]	X	X				
Photography		X	X	X		X
Randomization		X				
Treatment		X				
End of study[5]			X Group 2, powder BoNT-A			X Group 1, Alluzience
Investigator Assessments						
Reconstitution/Preparation Questionnaire		X				
Investigator Treatment Session Questionnaire[6]		X				
CCI [redacted]						

1. Screening and treatment/baseline visits can be performed at the same day
2. Only to be conducted if no screening visit has been performed. Changes to medical history should be asked for if the screening and baseline visits are not performed on the same day.
3. AEs are collected from treatment to the end of the subject's participation.
4. Only for women of childbearing potential
5. Subjects in the powder BoNT-A treatment group will be followed 1 month and subjects in the Alluzience treatment group will be followed for 6 months.
6. Only for Alluzience-treated subjects
7. Only to be completed once for each Treating Investigator, per study product, after all enrolled subjects have completed Visit 2.
8. Performed pre-treatment

Appendix B: Alluzience Preparation Questionnaire

Time for study product to equilibrate to room temperature
(*Note: should be 15 – 30 min according to CSP*)

☐☐☐☐
MM:SS

How long did it take to prepare the product to have it ready for injection?
Time from opening the outer box to having a syringe ready for use.

☐☐☐☐
MM:SS

Did you prepare the product in front of the subject? Yes ☐ No ☐

I did not experience any technical issues/problems when using a ready to use product as compared to a product to be reconstituted

Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
☐	☐	☐	☐	☐

Appendix C: BOTOX/Vistabel Reconstitution Questionnaire

Time for solvent to equilibrate to room temperature (*Note: should be 15 – 30 min according to CSP*)

☐☐☐☐
MM:SS

How long did it take to prepare the product to have it ready for injection?
Time from opening the outer box to having a syringe ready for use.

☐☐☐☐
MM:SS

Did you reconstitute in front of the subject? Yes ☐ No ☐

Any product problems associated with the reconstitution? Yes ☐ No ☐
If "Yes" above:

☐ Wrong final concentration (U/mL)
☐ Wrong concentration of NaCl used/wrong diluent used
☐ Vacuum not pulling the solvent into the vial
☐ Difficulties to insert the needle into the vial
☐ Particles in solution
☐ Bubble/Foam formation
☐ Waste of product
Other, please describe:_____

_____

_____

_____

Have you ever had any issues to reconstitute the powder BoNT-A in the past? Yes ☐
No ☐

If "Yes" above:

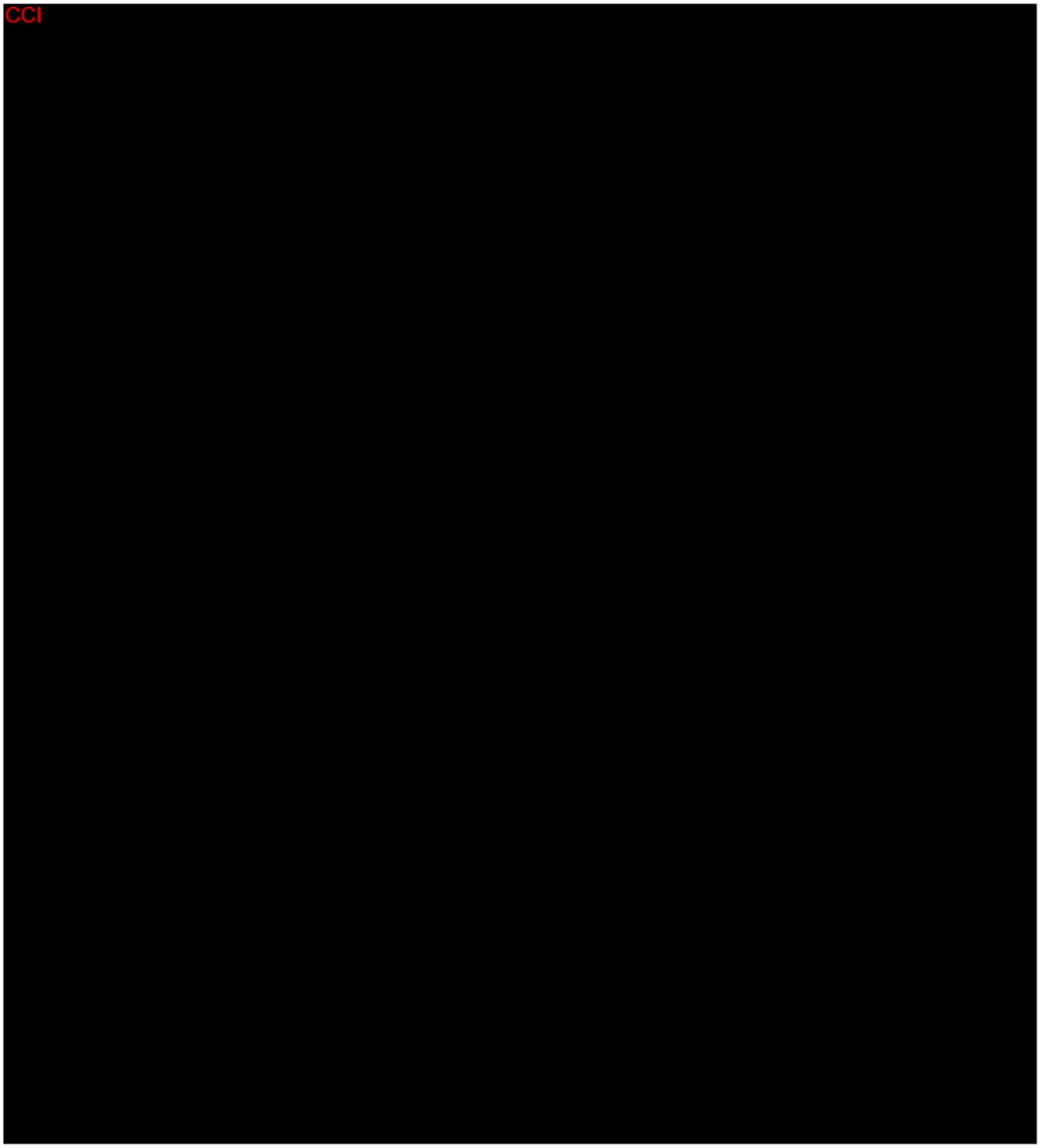
☐ Wrong final concentration (U/mL)
☐ Wrong concentration of NaCl used/wrong dilutient used
☐ Vacuum not pulling the solvent into the vial
☐ Difficulties to insert the needle into the vial
☐ Particles in solution
☐ Bubble/Foam formation
☐ Waste of product

Other, please describe:_____

Appendix D: Investigator Treatment Session Questionnaire (for Alluzience only)

NOTE: **To be answered for Alluzience only**	Strongly agree	Agree	Neither agree nor disagree	Disagree	Strongly disagree
1. I prefer to utilize a ready to use product as compared to a product to be reconstituted	❑	❑	❑	❑	❑
2. I could dedicate more time to explain the treatment procedure in using a ready to use product as compared to a product to be reconstituted	❑	❑	❑	❑	❑
3. I could save time on the reconstitution and injection procedure to do something else	❑	❑	❑	❑	❑
4. I felt more relaxed/less stressed in not having to reconstitute the product to be injected	❑	❑	❑	❑	❑
5. I feel more secure when I have a pre-diluted solution and don't have to reconstitute the product myself	❑	❑	❑	❑	❑
6. I have a good feeling about injecting a modern and innovative product as compared to the reconstituted product	❑	❑	❑	❑	❑
7. I feel I am more precise in my injection with a ready to use product compared to a product to be reconstituted	❑	❑	❑	❑	❑
8. I like to propose new innovative treatment with liquid ready to use product to my patient	❑	❑	❑	❑	❑
9. I produced substantially less waste of non-toxin material (syringes, needles, saline etc.) using ready-to-use product as compared to the reconstituted product	❑	❑	❑	❑	❑
10. When I use a ready to use toxin I spend less materials for injection	❑	❑	❑	❑	❑
11. I believe that the use of ready to use toxin is better for the environment as I produce less waste	❑	❑	❑	❑	❑
12. I feel more confident when injecting a product free from animal and human excipients	❑	❑	❑	❑	❑

CCI



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