Official Title:	**A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose Ranging Study of the Efficacy and Safety of INCB054707 Followed by an Extension Period in Participants With Vitiligo**
NCT Number:	NCT04818346
Document Date:	Statistical Analysis Plan: 25-April-2022

Statistical Analysis Plan

INCB 54707-205

A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of the Efficacy and Safety of INCB054707 Followed by an Extension Period in Participants With Vitiligo

IND Number:	[redacted]
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **United States**
Protocol Version:	**Protocol Amendment 2 dated 09 FEB 2022**
CRF Approval Date:	**28 JAN 2022**
SAP Version:	**Original**
SAP Author:	[redacted] [redacted]**Biostatistics**
Date of Plan:	**25 APR 2022**

This study is being conducted in compliance with Good Clinical Practice, including the archiving of essential documents.

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LIST OF ABBREVIATIONS

Abbreviations and Special Terms	Definition
AE	adverse event
ALT	alanine aminotransferase
AST	aspartate aminotransferase
BSA	body surface area
[redacted]	[redacted]
CI	confidence interval
[redacted]	[redacted]
CRF	case report form
[redacted]	[redacted]
CTCAE	Common Terminology Criteria for Adverse Events
DILI	drug-induced liver injury
[redacted]	[redacted]
DMC	data monitoring committee
ECG	electrocardiogram
eCRF	electronic case report form
[redacted]	[redacted]
[redacted]	[redacted]
F-BSA	facial body surface area
FDA	Food and Drug Administration
[redacted]	[redacted]
[redacted]	[redacted]
F-VASI	Facial Vitiligo Area Scoring Index
[redacted]	[redacted]
[redacted]	[redacted]
ITT	intent-to-treat
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	mixed-effects model for repeated measures
NCI	National Cancer Institute
NRI	nonresponder imputation
PC	placebo-controlled
[redacted]	[redacted]
[redacted]	[redacted]
PT	preferred term
PTA	pure-tone average

Abbreviations and Special Terms	Definition
QALYs	quality-adjusted life years
QD	once daily
QTcF	Fridericia's corrected QT interval
SAP	Statistical Analysis Plan
[redacted]	[redacted]
[redacted]	[redacted]
SOC	system organ class
[redacted]	[redacted]
T-BSA	total body surface area
TEAE	treatment-emergent adverse event
[redacted]	[redacted]
[redacted]	[redacted]
T-VASI	Total Vitiligo Area Scoring Index
[redacted]	[redacted]
[redacted]	[redacted]
ULN	upper limit of normal
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
WHO	World Health Organization
[redacted]	[redacted]

1. INTRODUCTION

This is a Phase 2, multicenter, randomized, parallel-group, placebo-controlled, double-blind, dose-ranging study to evaluate the efficacy and safety of INCB054707 (15, 45, and 75 mg QD) over a 24-week treatment period, followed by a 28-week double-blind extension period (INCB054707 45 mg and 75 mg QD). A safety follow-up visit will be conducted approximately 4 weeks after the last dose of study drug.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the INCB 54707-205 Protocol.

[redacted]

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 54707-205 Protocol Amendment 2 dated 09 FEB 2022 and CRFs approved 28 JAN 2022. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and eCRF versions.

2.2. Study Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
To determine the efficacy of INCB054707.	• Percent change from baseline in Total Vitiligo Area Scoring Index (T-VASI) at Week 24.
Key Secondary	
To further determine the efficacy of INCB054707.	• Proportion of participants achieving T-VASI50 at Week 24. T-VASI50 is defined as 50% or greater reduction in the Total Vitiligo Area Scoring Index.
Secondary	
To evaluate the safety and tolerability of INCB054707.	• Frequency and severity of AEs, including the results of physical examinations, vital signs, evaluation of clinical laboratory studies, and ECGs.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	

3. STUDY DESIGN

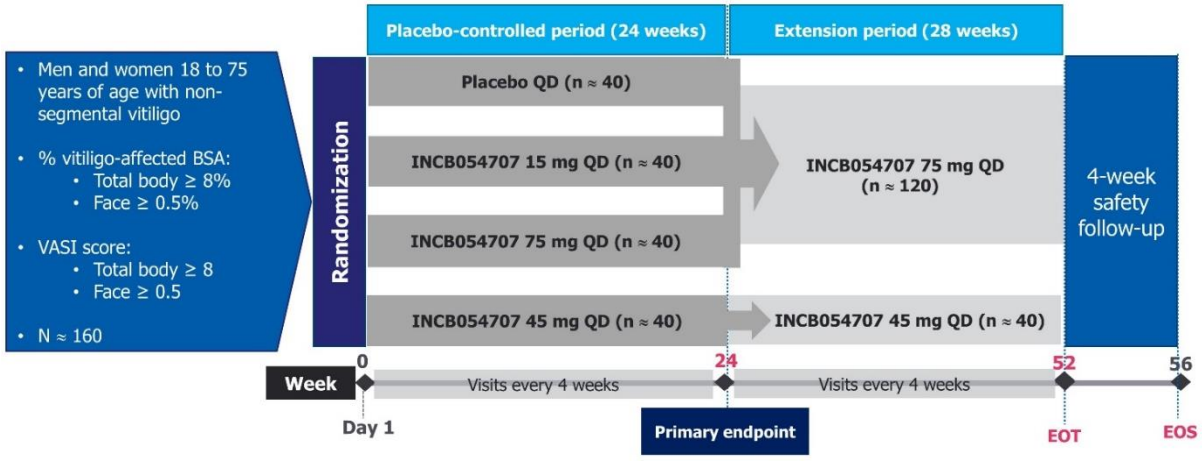
This is a Phase 2, multicenter, randomized, parallel-group, placebo-controlled, double-blind, dose-ranging study to evaluate the efficacy and safety of INCB054707 (15, 45, and 75 mg QD) over a 24-week double-blind PC period followed by a 28-week double-blind extension period (INCB054707 45 mg and 75 mg QD). The study will enroll approximately 160 men and women aged 18 to 75 years with nonsegmental vitiligo, with depigmented areas including T-BSA ≥ 8%, T-VASI ≥ 8, F-BSA ≥ 0.5%, and F-VASI ≥ 0.5.

Participants will be screened for up to 32 days before the first dose of study drug. Participants who meet all study entry criteria and none of the exclusion criteria will return to the study site on Day 1 of dosing and be randomized to 1 of 4 treatment groups. Participants will be stratified based on T-BSA involvement (8.0%-20.0% and > 20.0%).

Participants will receive double-blinded study treatment of placebo or 1 of 3 doses of INCB054707 (15, 45, or 75 mg) QD for 24 weeks. Participants who complete the Week 24 will enter the 28-week double-blind extension period with 45 mg QD (for participants who received 45 mg during the PC period) or 75 mg QD (for participants who received placebo, 15 mg, or 75 mg during the PC period), with a safety follow-up visit scheduled 4 weeks after the last dose of study drug.

The study schema is shown in Figure 1.

Figure 1: Study Design Schema



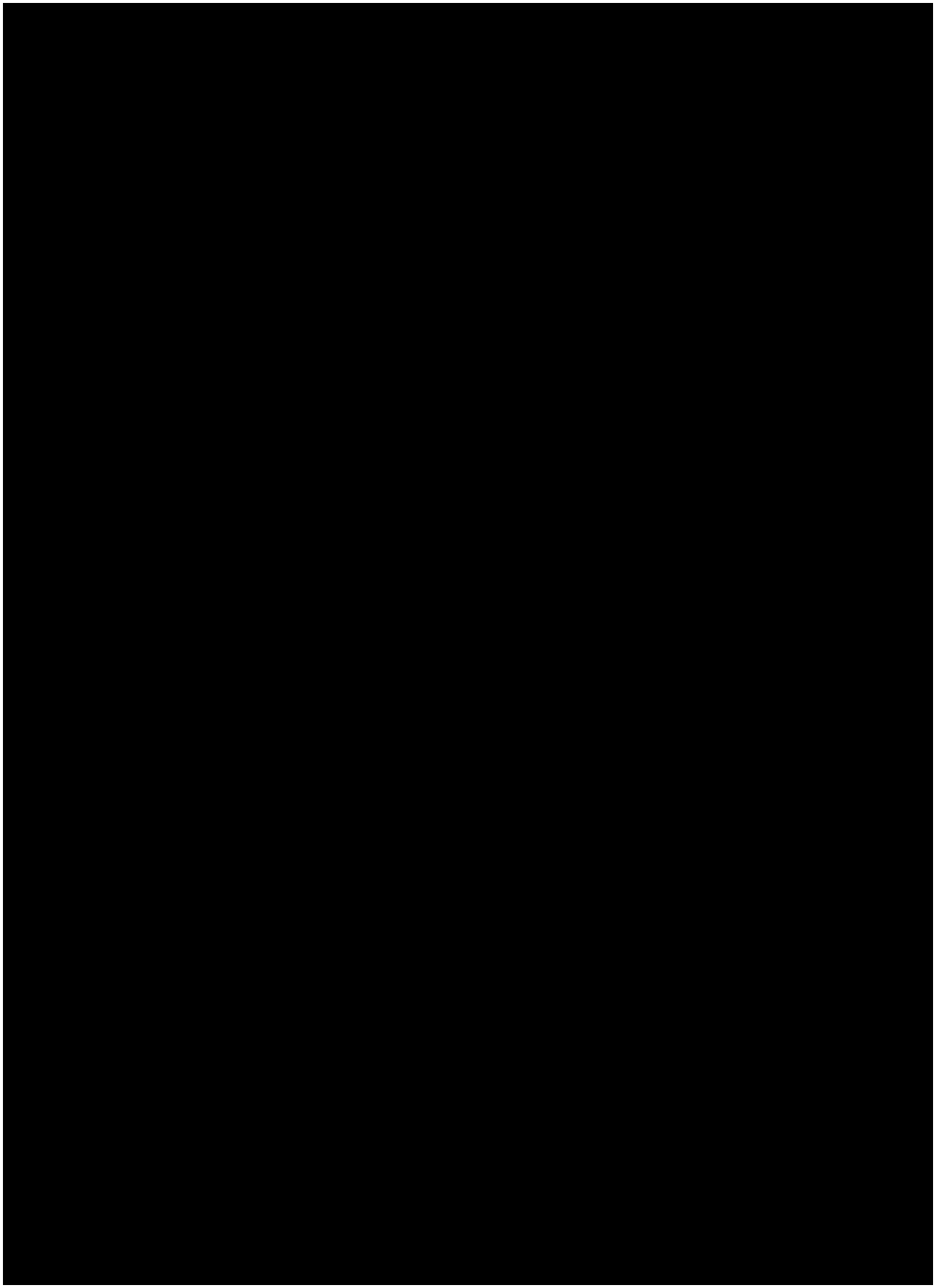
The primary analysis will occur after the primary database lock, when all participants have completed or discontinued from the PC, double-blind treatment period.

The final analysis will occur when all participants have completed or withdrawn from the study.

3.1. Randomization

Approximately 160 participants will be randomized 1:1:1:1 to 1 of 3 INCB054707 treatment groups or the placebo group (approximately 40 participants per group).

Participant randomization will be stratified based on T-BSA involvement (8.0%-20.0% and > 20.0%).



3.4. Schedule of Assessments

Refer to Protocol Amendment 2 dated 09 FEB 2022 for a full description of all study procedures and assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is defined in Table 2 for each period. Note that the treatment groups for each period are described in Section 5.2.

Table 2: Definition of Day 1

Treatment Period	Treatment Group	Day 1
PC period	Placebo INCB054707 15 mg INCB054707 45 mg INCB054707 75 mg	The day the first dose of study drug (INCB054707 or placebo) is administered to the participants in the PC period.
Extension period	Placebo to INCB054707 75 mg INCB054707 15 mg to 75 mg INCB054707 45 mg INCB054707 75 mg	The day the first dose of study drug (INCB054707 45 mg or 75 mg) is administered to the participants in the extension period.
Throughout study participation	INCB054707 45 mg INCB054707 75 mg	The day the first dose of study drug (INCB054707 45 mg or 75 mg) is administered to the participants in the PC period.

For randomized participants not treated with any study drug, Day 1 is defined as the day of randomization.

4.1.2. Study Day

If a visit/reporting date is on or after Day 1, then the study day at the visit/reporting date will be calculated as

Day # = (visit/reporting date – Day 1 date + 1).

If the visit/reporting date is before Day 1, then the study day at the visit/reporting date will be calculated as

Day # = (visit/reporting date – Day 1 date).

A study day of –1 indicates 1 day before Day 1.

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained before the first administration of INCB054707 or placebo in the PC period, unless otherwise defined.

For randomized participants not treated with any study drug, baseline is defined as the last nonmissing assessment before or on the day of randomization for all parameters.

For participants who continue in the extension period, baseline is defined as follows:

- For efficacy evaluation in the extension period, baseline is the last nonmissing measurement obtained before the first administration of study drug in the PC period, unless otherwise defined.
- For safety evaluation in the extension period, baseline is the last nonmissing measurement obtained before the first administration of study drug in the extension period, unless otherwise defined.

When scheduled assessments and unscheduled assessments occur on the same day and the time of the assessment or time of first dose is not available, use the following convention to determine baseline:

- If both a scheduled and an unscheduled visit are available on the day of the first dose and the time is missing, use the scheduled assessment as baseline.
- If all scheduled assessments are missing on the day of the first dose and an unscheduled assessment is available, use the unscheduled assessment as baseline.

4.1.4. Handling of Missing and Incomplete Dates

In general, values for missing dates will not be handled unless methods for handling missing dates are specified in this section or relevant sections. The original reported dates collected in the eCRF should be used in all relevant listings. The following rules will be used for handling partial dates for analyses requiring dates.

When calculating the time since diagnosis of nonsegmental vitiligo, a partial diagnosis date will be handled as follows in the calculation:

- If only the day is missing, then the first day of the month will be used.
- If both the month and day are missing, then 01 JAN of the year will be used.
- If the diagnosis date is completely missing, then the time since diagnosis will not be calculated.

When the date of the last dose is used in deriving variables such as duration of treatment or TEAE flag, a missing or partial date of the last dose will be handled as follows:

- If only the day is missing, then the earlier date of the last day of the month or the date that the participant discontinued treatment will be used.
- If both the month and day are missing, then the earlier date of 31 DEC of the year or the date that the participant discontinued treatment will be used.
- Otherwise, the date that the participant discontinued treatment will be used as the date of the last dose.

4.2. Variable Definitions

The following variables will only be calculated if not reported in the eCRF.

4.2.1. Body Mass Index

Body mass index will be calculated as follows:

Body mass index (kg/m^2) = [weight (kg)] / [height (m)]^2.

4.2.2. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of INCB054707 or placebo in the PC period.

In the PC period, concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first administration of INCB054707 or placebo in the PC period and is ongoing throughout the study or ends on/after the date of first study drug administration during the PC period.
- On/after the date of first administration of INCB054707 or placebo in the PC period and is ongoing or ends during the PC period.

In the extension period, concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first administration of INCB054707 in the extension period and is ongoing throughout the study or ends on/after the date of first study drug administration during the extension period.
- On/after the date of first administration of INCB054707 in the extension period and is ongoing or ends during the extension period.

A prior medication could also be classified as "both prior and concomitant medication" if the end date is on or after first dose of INCB054707 or placebo. In the listing, it will be indicated whether a medication is only prior, only concomitant, or both prior and concomitant.

For the purposes of analysis, all medications will be considered concomitant medications unless the medications can unequivocally be defined as not concomitant.

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9.1 or later) will be used for the generation of all tables, graphs, and statistical analyses. Descriptive summaries for continuous variables will include but not be limited to the number of observations, mean, standard deviation, median, minimum, and maximum. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

5.2. Treatment Groups

This is a randomized, double-blind, placebo-controlled, dose-ranging study followed by a double-blind extension period. Table summaries, unless otherwise indicated, will present data by treatment group. The results will be summarized and presented separately for the PC period and the extension period, unless otherwise specified.

For the PC period, the treatment groups will be placebo and INCB054707 15, 45, and 75 mg.

For the extension period, the participants will be grouped as follows according to the treatment they received during the PC period:

- Placebo to INCB054707 75 mg
- INCB054707 15 mg to 75 mg
- INCB054707 45 mg
- INCB054707 75 mg

5.3. Analysis Populations

5.3.1. All-Randomized Population

The all-randomized population will include all participants who were randomized.

5.3.2. Intent-to-Treat Population

All participants who were randomized to the study constitute the ITT population. Treatment groups for this population will be defined according to the treatment assignment at the time of randomization regardless of the actual study treatment the participant might apply during their participation in the PC period.

The ITT population will be used for the summary of demographics, baseline characteristics, participant disposition, and analyses of all efficacy data in the PC period.

5.3.3. Safety Population

The safety population will include all participants who received at least 1 dose of INCB054707 or placebo during the PC period. Treatment groups for this population will be determined according to the actual treatment the participant receives on Day 1 in the PC period regardless of assigned study treatment.

All safety analyses for the PC period will be conducted using the safety population.

5.3.4. Extension Evaluable Population

All analyses for the extension period will be conducted with the extension evaluable population, which includes all participants who received at least 1 dose of INCB054707 during the extension period.

6. BASELINE, EXPOSURE, AND DISPOSITION

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

6.1. Demographics, Baseline Characteristics, and Disease History

Demographics, baseline characteristics, and disease history will be summarized by treatment group and overall.

6.1.1. Demographics and Baseline Characteristics

The following demographics will be summarized for the ITT population and the extension evaluable population: age, sex, race, ethnicity, weight, height, BMI, and BMI category (< 25 kg/m^2, ≥ 25 to < 30 kg/m^2, ≥ 30 to < 40 kg/m^2, ≥ 40 to < 50 kg/m^2, ≥ 50 kg/m^2).

The following demographics will be summarized for the ITT population only: tobacco use (never used, current user, former user).

6.1.2. Baseline Disease Characteristics and Disease History

The baseline disease characteristics and disease history summarized for all participants in the ITT population include but are not limited to the following:

- Disease duration (years)
- Fitzpatrick scale skin type (Type I, II, III, IV, V, VI)
- Vitiligo family history
- Prior therapy or surgery for vitiligo treatment
- Selected comorbidities
- Baseline F-BSA involvement
- Baseline F-BSA involvement category (≤ 0.5%, > 0.5%-1.0%, > 1.0%-1.5%, > 1.5%-2.0%, > 2.0%-2.5%, > 2.5%-3.0%)

[redacted]

- Baseline T-BSA involvement
- Baseline T-BSA involvement category (≤ 8.0%, > 8.0%-14.0%, > 14.0%-20.0%, > 20.0%-30.0%, > 30.0%-40.0%, > 40.0%-50.0%, > 50.0%-80.0%, > 80.0%)
- Baseline T-BSA involvement stratification category (8.0%-20.0%, > 20.0%)
- Baseline T-VASI score
- Baseline T-VASI score category (≤ 8.0, > 8.0-14.0, > 14.0-20.0, > 20.0-30.0, > 30.0-40.0, > 40.0-50.0, > 50.0-80.0, > 80.0)
- [redacted]
- [redacted]
- History of acne vulgaris (no/yes)
- Currently having acne vulgaris (no/yes)
- Vitiligo in genital area (no/yes)
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]
- [redacted]

Note: disease duration (years) will be calculated as follows:

disease duration (years) = (date of randomization − date of diagnosis + 1) / 365.25.

[redacted]

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

[redacted]

6.1.3. Medical History

For participants in the ITT population, medical history will be summarized by assigned treatment group. This summary will include the number and percentage of participants with medical history for each body system/organ class as documented in the eCRF.

6.2. Disposition of Participant

The number of participants enrolled by country and/or site will be summarized for the ITT population by treatment group and overall.

The following will be summarized by treatment group and overall for the ITT population in the PC period:

- Number (%) of participants who were randomized
- Number (%) of participants who were treated in the PC period
- Number (%) of participants who completed treatment in the PC period through Week 24
- Number (%) of participants who discontinued study treatment in the PC period with a primary reason for discontinuation
- Number (%) of participants who withdrew from the study in the PC period with a primary reason for withdrawal

The following will be summarized by treatment group and overall for the extension evaluable population in the extension period:

- Number (%) of participants who were treated in the extension period
- Number (%) of participants who completed treatment in the extension period
- Number (%) of participants who discontinued study treatment in the extension period with a primary reason for discontinuation
- Number (%) of participants who completed the study
- Number (%) of participants who withdrew from the study in the extension period with a primary reason for withdrawal

6.3. Protocol Deviations

Protocol deviations recorded will be summarized by treatment group and overall, for the ITT population in the PC period and the extension evaluable population in the extension period, and listed.

6.4. Exposure

For participants in the safety population in the PC period, the extension evaluable population in the extension period, and those who took INCB054707 45 mg or 75 mg throughout study participation, study drug exposure will be summarized by treatment group descriptively as the following:

- **Duration of treatment with study drug (days)**: date of last dose of study drug in the specific period – date of first dose of study drug in the specific period + 1.

The date of first and last doses of study drug in each period are defined in Table 3.

Table 3: Definition of First and Last Dose Date

Treatment Period	Treatment Group	First Dose Date	Last Dose Date
PC period	Placebo INCB054707 15 mg INCB054707 45 mg INCB054707 75 mg	Date that the first dose of study drug was administered to the participants in the PC period	Date that the last dose of study drug was administered to the participants in the PC period
Extension period	Placebo to INCB054707 75 mg INCB054707 15 mg to 75 mg INCB054707 45 mg INCB054707 75 mg	Date that the first dose of study drug was administered to the participants in the extension period	Date that the last dose of study drug was administered to the participants in the extension period
Throughout study participation	INCB054707 45 mg INCB054707 75 mg	Date that the first dose of study drug was administered to the participants in the PC period	Date that the last dose of study drug was administered to the participants throughout study participation

In addition, for the safety population in the PC period and the extension evaluable population in the extension period, average daily dose of INCB054707 and total actual dose of INCB054707 will be summarized by treatment group descriptively as follows:

- **Average daily dose of INCB054707 (mg/day)**: total actual INCB054707 dose taken in the specific period (mg) / [duration of treatment with INCB054707 in the specific period (days) – number of interrupted days with INCB054707 in the specific period].
- **Total actual dose of INCB054707 taken (mg)**: (total number of tablets dispensed in the specific period – total number of tablets returned in the specific period) × 15 (mg/tablet) × p_T

  in which p_T denotes the proportion of INCB054707 among the 5 tablets taken daily with $p_T = 0$ (0/5) for the placebo group, 1/5 for the INCB054707 15 mg group, 3/5 for the INCB054707 45 mg group, and 1 (5/5) for the INCB054707 75 mg group.

The total number of tablets dispensed and returned in each period is based on information entered in the Drug Accountability eCRF. If there is dispensed drug that has not been returned, the actual dose taken starting from the dispense date of the unreturned drug will be imputed by the dose taken as reported in the Compliance eCRF.

6.5. Study Drug Compliance

For participants in the safety population and the extension evaluable population, the overall compliance (%) for INCB054707/placebo will be calculated for all participants as follows:

compliance (%) = 100 × [total dose actually taken in the specific period] / [total prescribed dose in the specific period].

The total prescribed dose in the specific period is defined as the sum of the doses prescribed by the investigator accounting for dose interruptions during the specific period, and will be calculated as: [duration of treatment with study drug in the specific period − number of days with dose interruptions in the specific period] × 5 (tablets/day).

The total dose actually taken in the specific period will be calculated as: total number of tablets dispensed in the specific period − total number of tablets returned in the specific period (see Section 6.4 for details on total number of tablets dispensed and returned).

6.6. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary. For the ITT population in the PC period, both prior and concomitant medications will be summarized by treatment group and overall. For the extension evaluable population in the extension period, only concomitant medication will be summarized by treatment group and overall. All summaries will be by WHO drug class and WHO drug preferred term.

7. EFFICACY

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

7.1. General Considerations

All by-visit analyses for the extension evaluable population will include the follow-up period if the data are available, unless otherwise specified.

Unless otherwise stated, the strata identified in the randomization process will be used in all efficacy analyses.

[redacted]

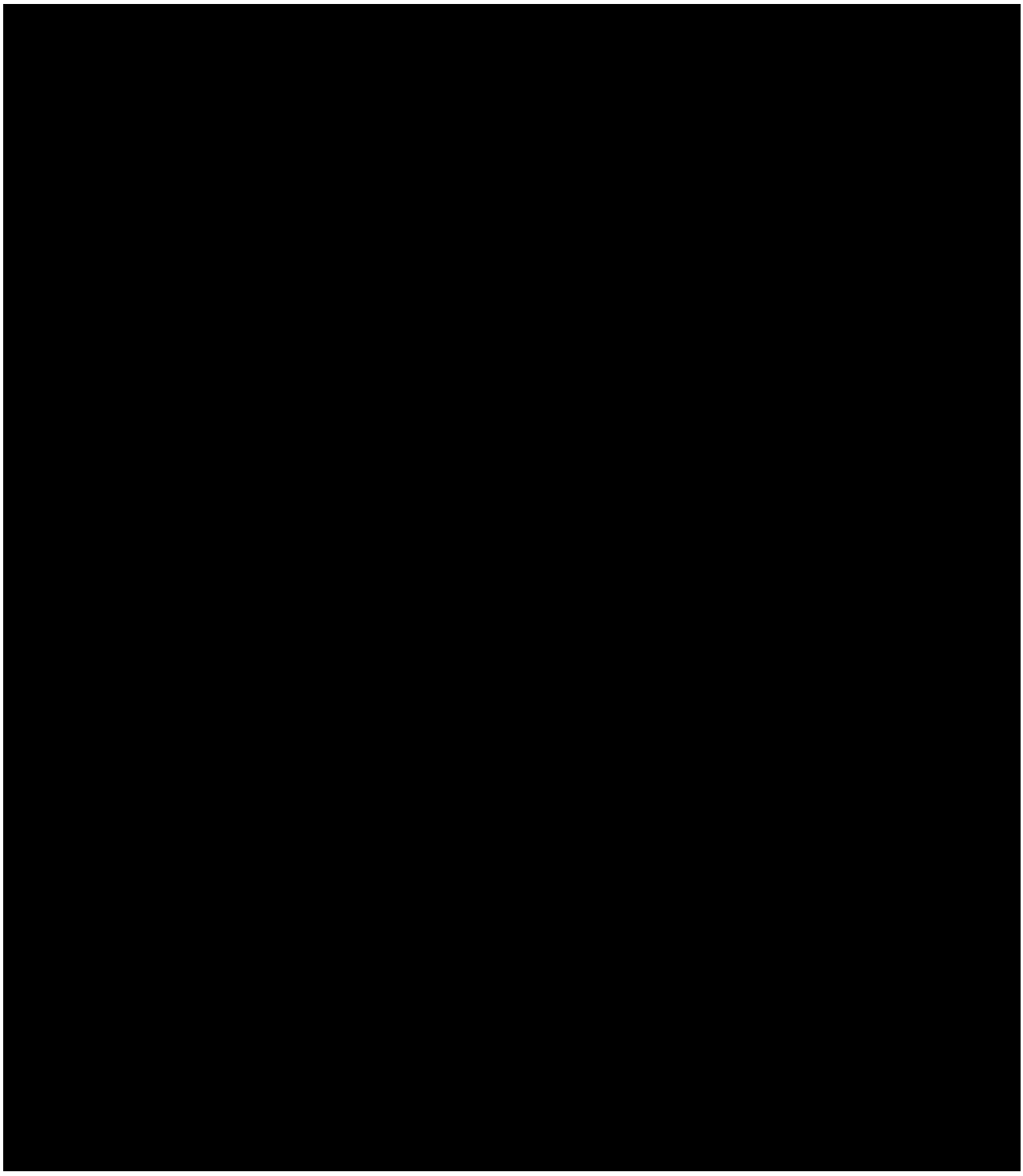
Total body VASI (T-VASI) is calculated using a formula that includes contributions from all body regions (possible range: 0-100) as follows:

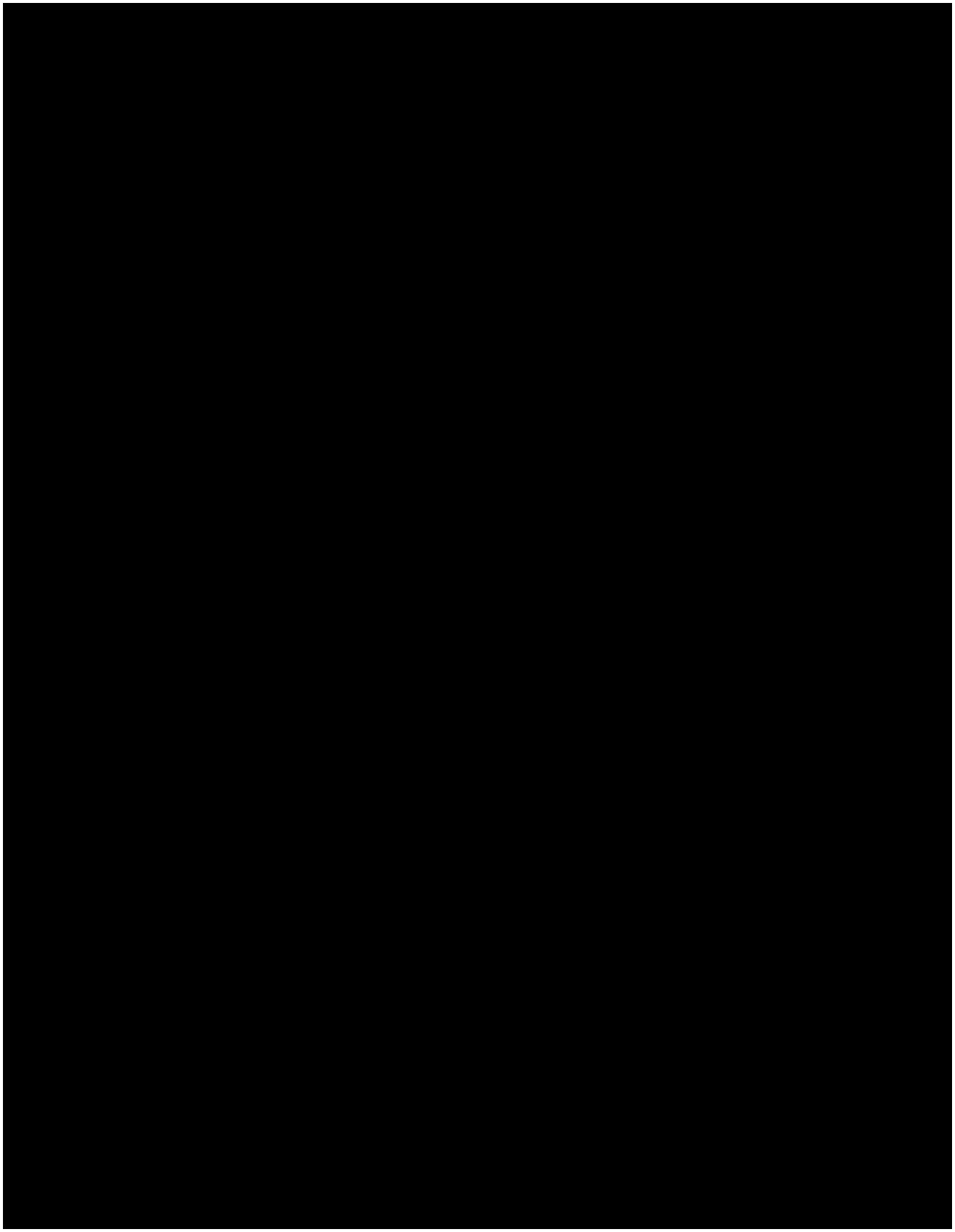
$$\text{VASI} = \sum_{\text{all body sites}} [\text{Hand Units}] \times [\text{Residual Depigmentation}]$$

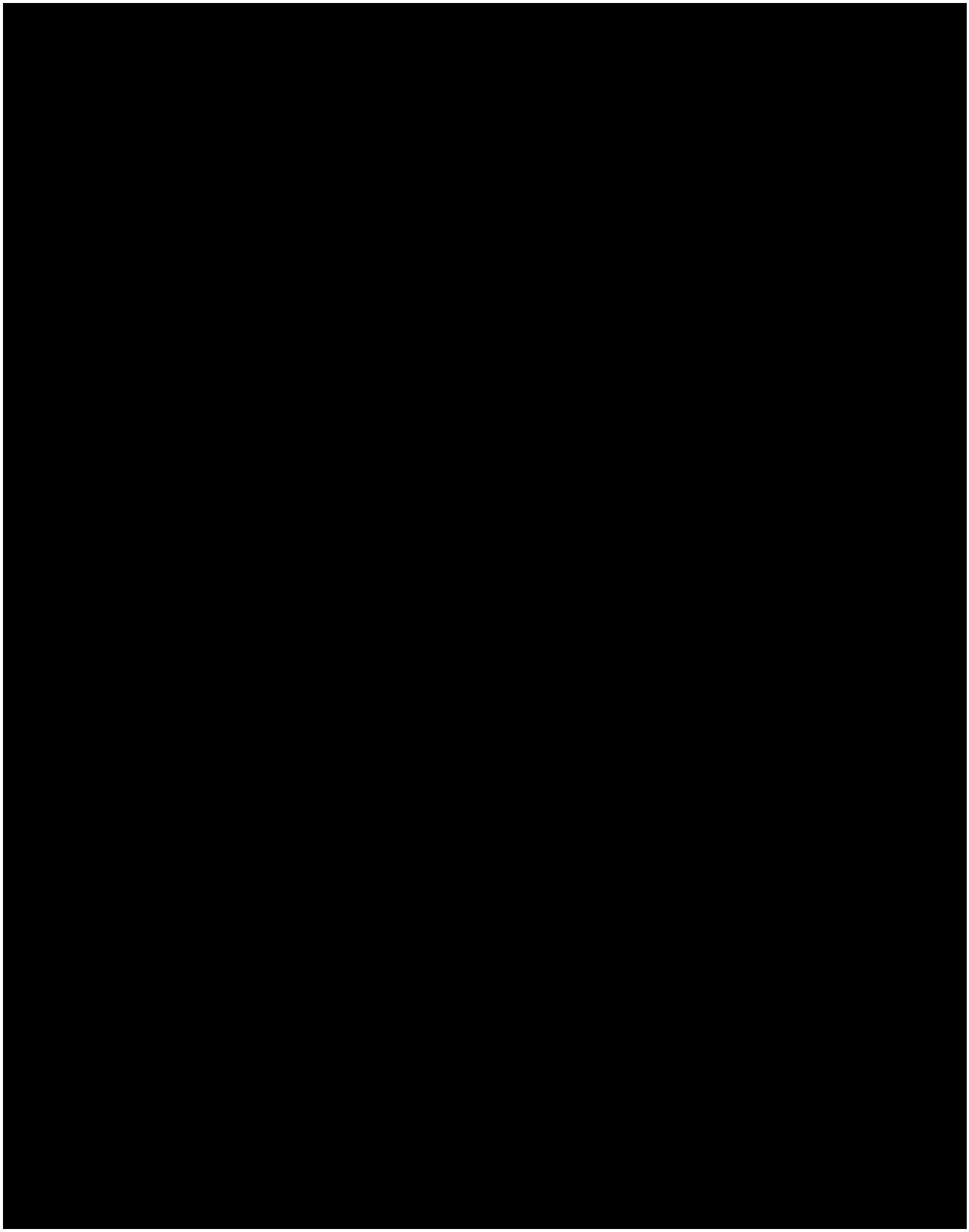
The body is divided into the following 6 separate and mutually exclusive sites: (1) head/neck, (2) hands, (3) upper extremities (excluding hands), (4) trunk, (5) lower extremities (excluding feet), and (6) feet. The percentage of vitiligo involvement is estimated in hand units (%BSA) by the same investigator during the entire course of the study. Hand unit is based on the participant's hand size. The investigator uses their hand to mimic the participant's hand size to evaluate %BSA vitiligo involvement. The degree of depigmentation for each body site is determined and estimated to the nearest of the following percentages: 0%, 10%, 25%, 50%, 75%, 90%, or 100%. The T-VASI is then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each body site and summing the values of all body sites together (Hamzavi et al 2004).

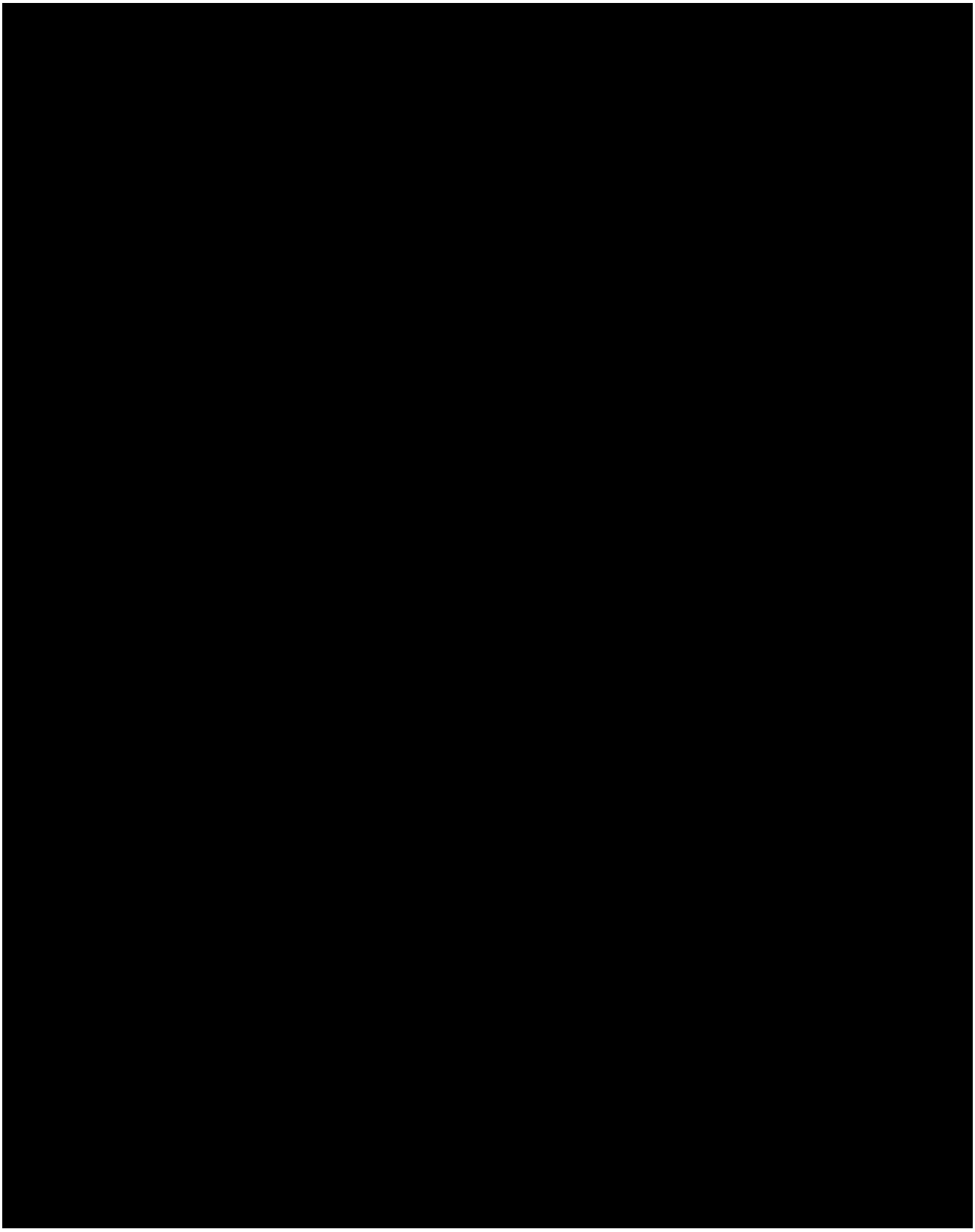
The T-VASI50 is defined as at least 50% reduction from baseline in T-VASI. [redacted]

[redacted]

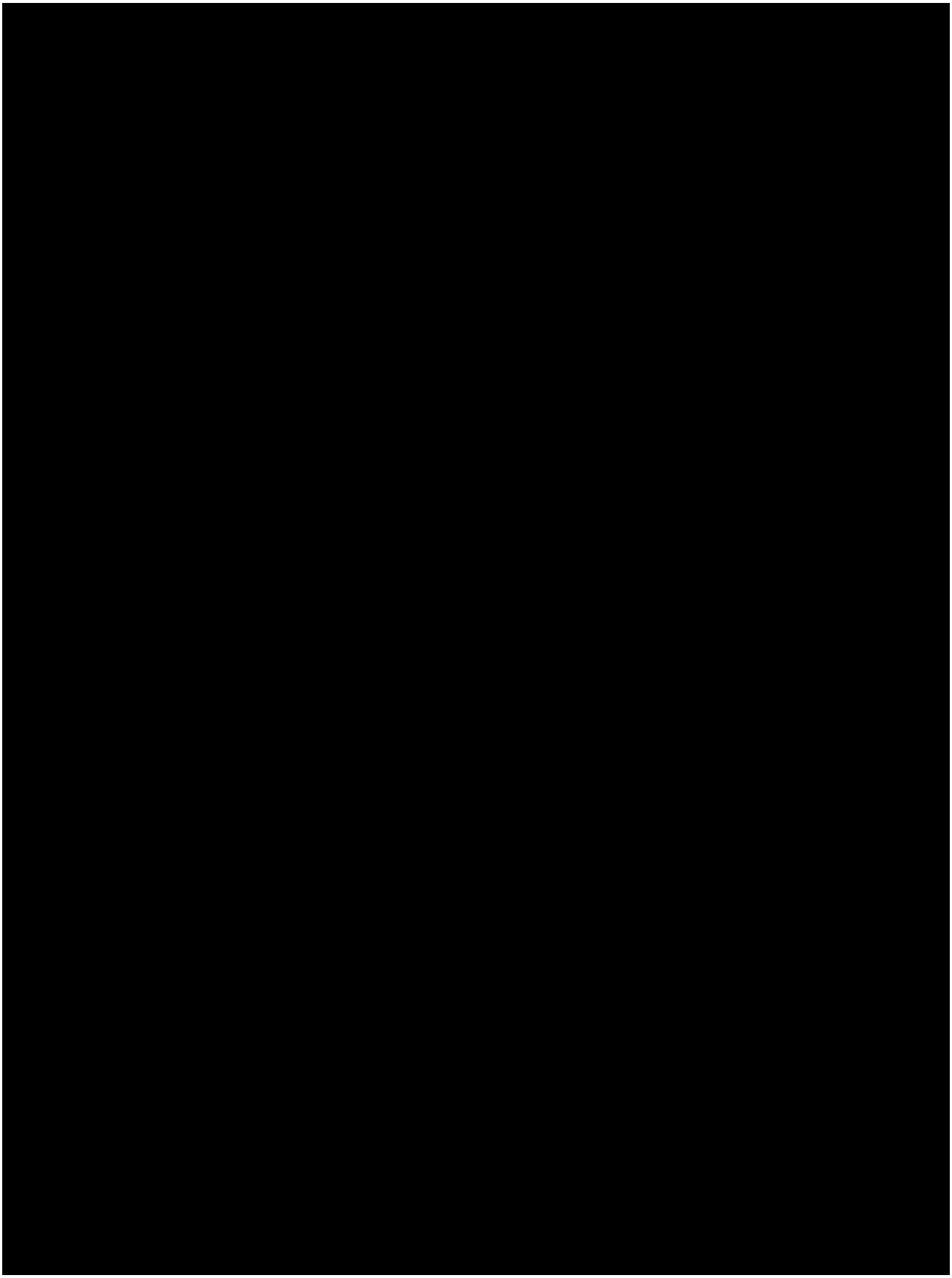








[redacted]



[redacted]

7.3. Efficacy Hypotheses

The primary hypothesis is that INCB054707 75 mg is superior to placebo at Week 24 in mean percent change from baseline in T-VASI in participants with vitiligo. Assuming μ_T is the mean percent change from baseline at Week 24 in T-VASI in the INCB054707 75 mg group and μ_C is the mean percent change from baseline at Week 24 in T-VASI in the placebo group, the primary hypotheses of the study are as follows:

- H_0 (null hypothesis): $\mu_T = \mu_C$
- H_A (alternative hypothesis): $\mu_T \neq \mu_C$

7.4. Analysis of the Primary Efficacy Parameter

The primary efficacy endpoint is the percent change from baseline in T-VASI at Week 24.

7.4.1. Primary Efficacy Analysis

[redacted]

[redacted]

[redacted]

7.4.2. Subgroup Analyses for Primary Endpoint

A subgroup will be formed based on the following participant characteristics and baseline variables for those participants whose data are available:

- Baseline T-BSA involvement (8.0%-20.0%, > 20.0%)

The primary efficacy endpoint will be summarized using descriptive statistics based on the ITT population for the subgroups defined above.

7.4.3. Sensitivity and Supportive Analyses for Primary Endpoint

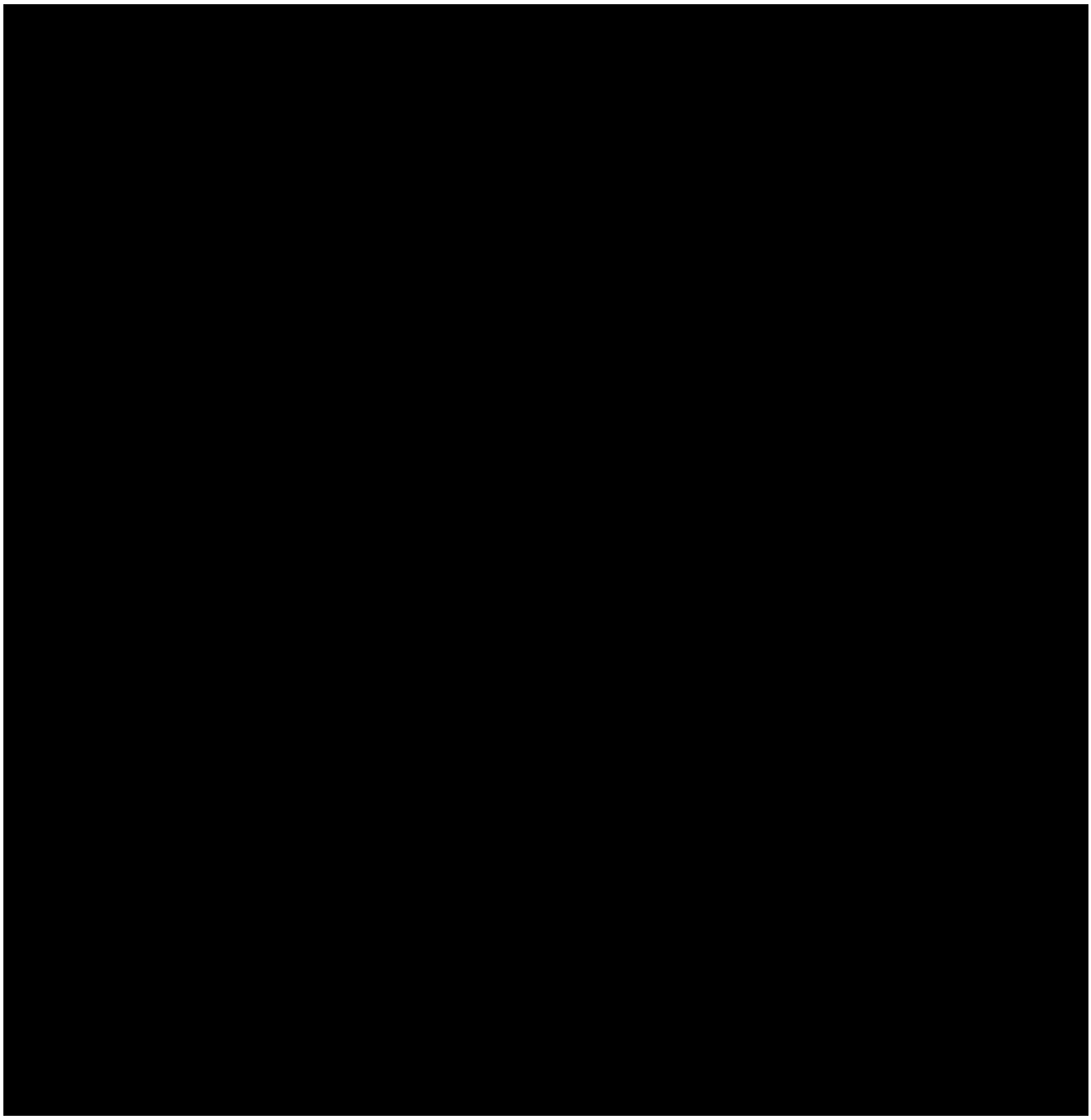
Not applicable.

7.5. Analysis of the Secondary Efficacy Parameters

The key secondary efficacy endpoint is proportion of participants who achieve T-VASI50 at Week 24.

[redacted]

[redacted]



8. SAFETY AND TOLERABILITY

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

8.1. General Considerations

The analyses in this section will be provided for the safety population in the PC period and the extension evaluable population in the extension period unless otherwise specified. Summary tables may be replaced with listings when appropriate. For instance, an AE frequency table may be replaced with a listing if it only contains a few unique PTs reported on relatively few participants.

8.2. Adverse Events

8.2.1. Adverse Event Definitions

A TEAE is any AE either reported for the first time or worsening of a pre-existing event after the first dose of study drug until the end of the safety follow-up.

A TEAE in the PC period is any AE with a start time after the first dose of study drug in the PC period and until the end of the safety follow-up, or prior to the first dose in the extension period for participants who entered in to the extension period.

A TEAE in the extension period is any AE with a start time after the first dose of study drug in the extension period until the end of the safety follow-up.

For participants who took INCB054707 45 mg or 75 mg throughout study participation, a TEAE is any AE with a start time after the first dose of study drug in the PC period until the end of the safety follow-up.

Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study drug administration. For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment-emergent.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the NCI CTCAE v5.0. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

The subset of AEs considered by the investigator to be related to study drug will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study drug, the AE will be considered to be treatment-related. The incidence of AEs and treatment-related AEs will be tabulated. In addition, serious TEAEs will also be tabulated.

8.2.2. Adverse Event Summaries

Adverse events will be summarized by treatment group and overall INCB054707 dose groups for the safety population in the PC period. For the extension evaluable population in the extension

period and for participants who took INCB054707 45 mg or 75 mg throughout study participation, AEs will be summarized by treatment group and overall.

An overall summary of AEs will include the following:

- Number (%) of participants reporting any TEAEs
- Number (%) of participants reporting any serious TEAEs
- Number (%) of participants reporting any Grade 3 or higher TEAEs
- Number (%) of participants reporting any treatment-related TEAEs
- Number (%) of participants who temporarily interrupted study treatment because of TEAEs
- Number (%) of participants who permanently discontinued study treatment because of TEAEs
- Number (%) of participants who had a fatal TEAE

The following summaries will be produced by MedDRA term (if 10 or fewer participants appear in a table, a listing may be appropriate):

- Summary of TEAEs by MedDRA SOC and PT
- Summary of TEAEs by MedDRA PT in decreasing order of frequency
- Summary of TEAEs by MedDRA SOC, PT, and maximum severity
- Summary of TEAEs by MedDRA SOC, PT, and CTCAE grade category
- Summary of Grade 3 or higher TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or higher TEAEs by MedDRA PT in decreasing order of frequency
- Summary of serious TEAEs by MedDRA SOC and PT
- Summary of serious TEAEs by MedDRA PT in decreasing order of frequency
- Summary of treatment-related TEAEs by MedDRA SOC and PT
- Summary of treatment-related TEAEs by MedDRA PT in decreasing order of frequency
- Summary of Grade 3 or higher treatment-related TEAEs by MedDRA SOC and PT
- Summary of treatment-related serious TEAEs by MedDRA SOC and PT
- Summary of TEAEs with a fatal outcome by MedDRA SOC and PT
- Summary of TEAEs leading to dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of study drug by MedDRA SOC and PT
- Summary of TEAEs requiring concomitant medications by MedDRA SOC and PT

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

Laboratory values, change from baseline values, and percent change from baseline values will be summarized descriptively by visit, and non-numeric test values will be tabulated when necessary. Baseline will be determined according to Section 4.1.3. The last record before study drug administration in the highest priority will be considered the baseline record. For baseline laboratory candidates with the same date and time in the same priority category, additional rules may be provided after consultation with the medical monitor to delineate which value will be defined as baseline.

8.3.2. Laboratory Value Summaries

All test results and associated normal ranges from central laboratories will be reported in SI units. All tests with numeric values will have a unique unit per test. Any laboratory test results and associated normal ranges from local laboratories will be converted to SI units.

When there are multiple laboratory nonmissing values for a participant's particular test at a scheduled visit, central laboratory values have higher priority over local laboratory values. If a tie still exists, the laboratory value with the smallest laboratory sequence number will be used in by-visit summaries. In addition, box-and-whisker plots will be provided for creatine kinase, hemoglobin, hematocrit, platelet count, high sensitivity C-reactive protein, lymphocyte absolute count, neutrophil absolute count, white blood cell count, total cholesterol, HDL, LDL, and HDL/LDL ratio.

For test results that will be summarized with available normal ranges, the number and percentage of participants with the laboratory values being low (but never high), normal, high (but never low), and both low and high will be calculated for each test. This shift summary will be produced for each test. The denominator for the percentage calculation will use the number of participants in the baseline category (ie, low, high, normal, missing) as the denominator for the percentage in each of the categories during the study.

Severity grades will be assigned to laboratory test values based on the numerical component of CTCAE v5. Shift tables will also be presented showing change in CTCAE grade from baseline to the worst grade postbaseline. Separate summaries for abnormally high and abnormally low laboratory values will be provided when the laboratory parameter has both high and low grading criteria. The denominator for the percentage calculation will be the number of participants in the baseline category. The number of participants who experienced worsening of laboratory abnormalities will be summarized by maximum severity.

8.3.3. Potentially Clinically Important Laboratory Values

Criteria for potentially clinically important laboratory values are listed in Table 6.

[redacted]

8.4. Vital Signs

Values at each scheduled visit, change, and percentage change from baseline for vital signs, including blood pressure, pulse, respiratory rate, and body temperature will be summarized descriptively. Baseline will be determined according to Section 4.1.3.

Normal ranges for vital sign values are defined in Table 7. For participants exhibiting vital sign abnormalities, the abnormal values will be listed along with their assigned treatment group. Alert vital signs are defined as an absolute value outside the defined range and percentage change greater than 25%. Note that the definition of alert vital signs does not apply to body temperature. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

8.5. Electrocardiograms

Twelve-lead ECGs including PR, QT, QRS, and QTcF intervals will be obtained for each participant during the study. Values at each scheduled visit, change, and percentage change from baseline will be summarized for each ECG parameter. Baseline will be determined as the average of all nonmissing values before the first administration of INCB054707 or placebo.

Normal ranges for ECG values are defined in Table 8. Electrocardiogram values will also be considered abnormal if the absolute percentage change from baseline is more than 25% (30% for QRS interval). Participants exhibiting ECG abnormalities will be listed with study visit and assigned treatment group. Abnormal values for participants with alert ECG values, defined as both the absolute value and the percentage change from baseline being outside normal ranges,

will be identified and listed. Outliers of QT and QTcF values, defined as absolute values > 450 milliseconds, > 500 milliseconds, or change from baseline > 30 milliseconds, will be summarized.

[redacted]

9. INTERIM ANALYSES

There are no planned, formal interim analyses for this study. An external DMC will be charged with evaluating interim safety results. The sponsor will remain blinded, and DMC decisions will be communicated through sponsor management as dictated in the DMC charter. Additional operational details of the interim analyses, including tables, figures, and listings provided to the DMC, will be documented in the DMC charter. Additional safety analyses may be performed at the discretion of the DMC chair.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 9.

Table 9: Statistical Analysis Plan Versions

SAP Version	Date
Original	25 APR 2022

10.1. Changes to Protocol-Defined Analyses

[redacted]

10.2. Changes to the Statistical Analysis Plan

Not applicable.

11. REFERENCES

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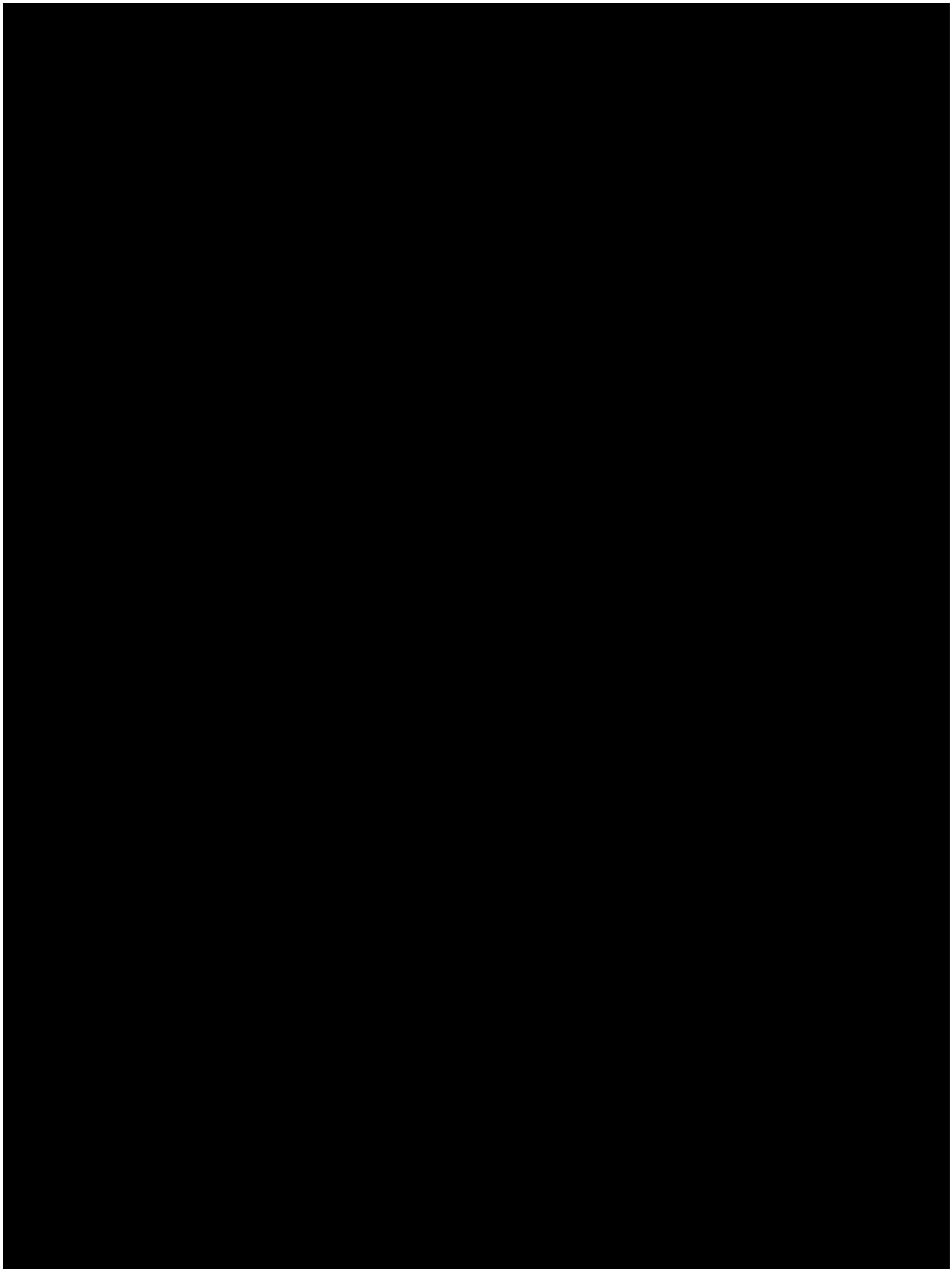

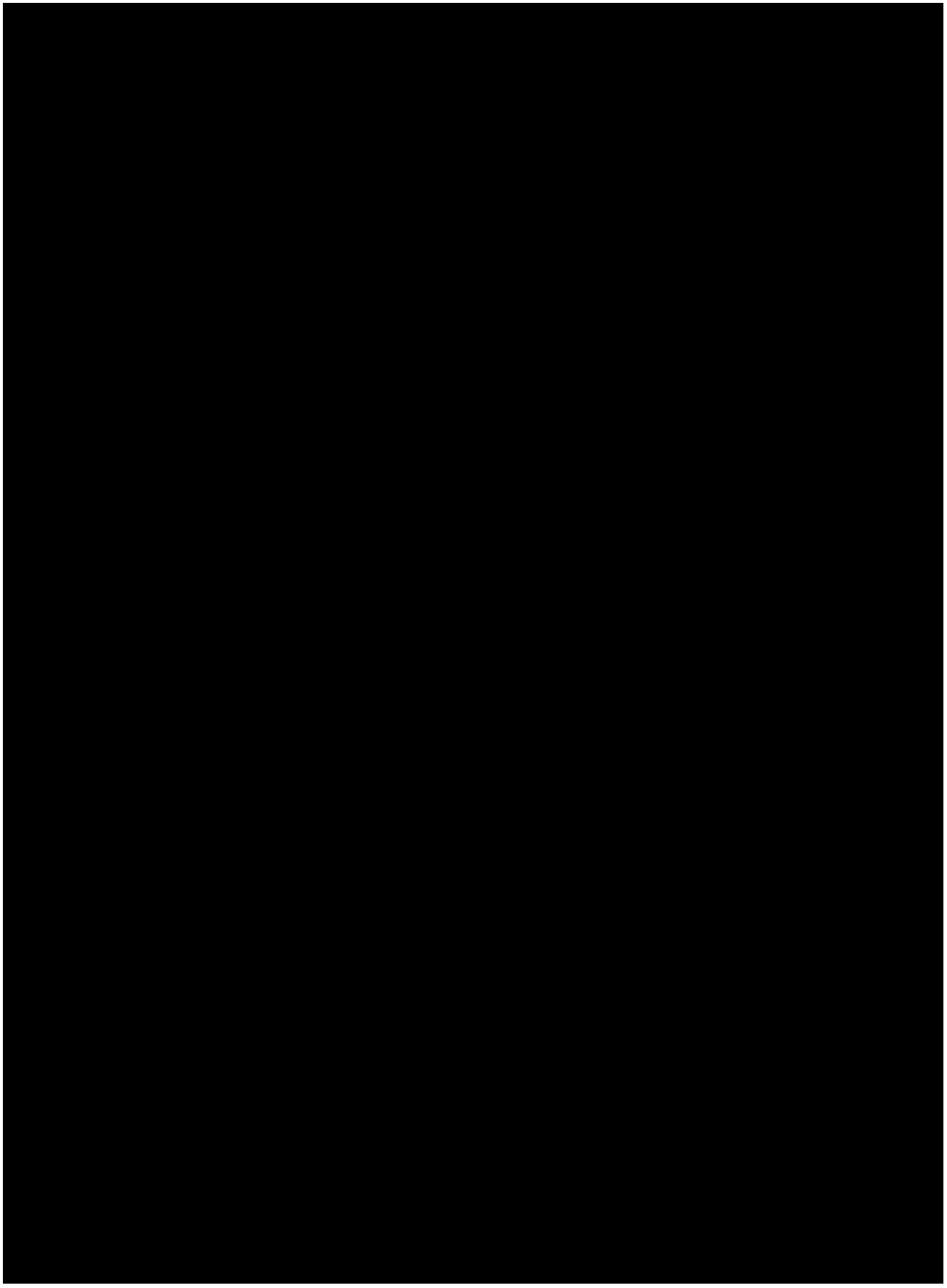

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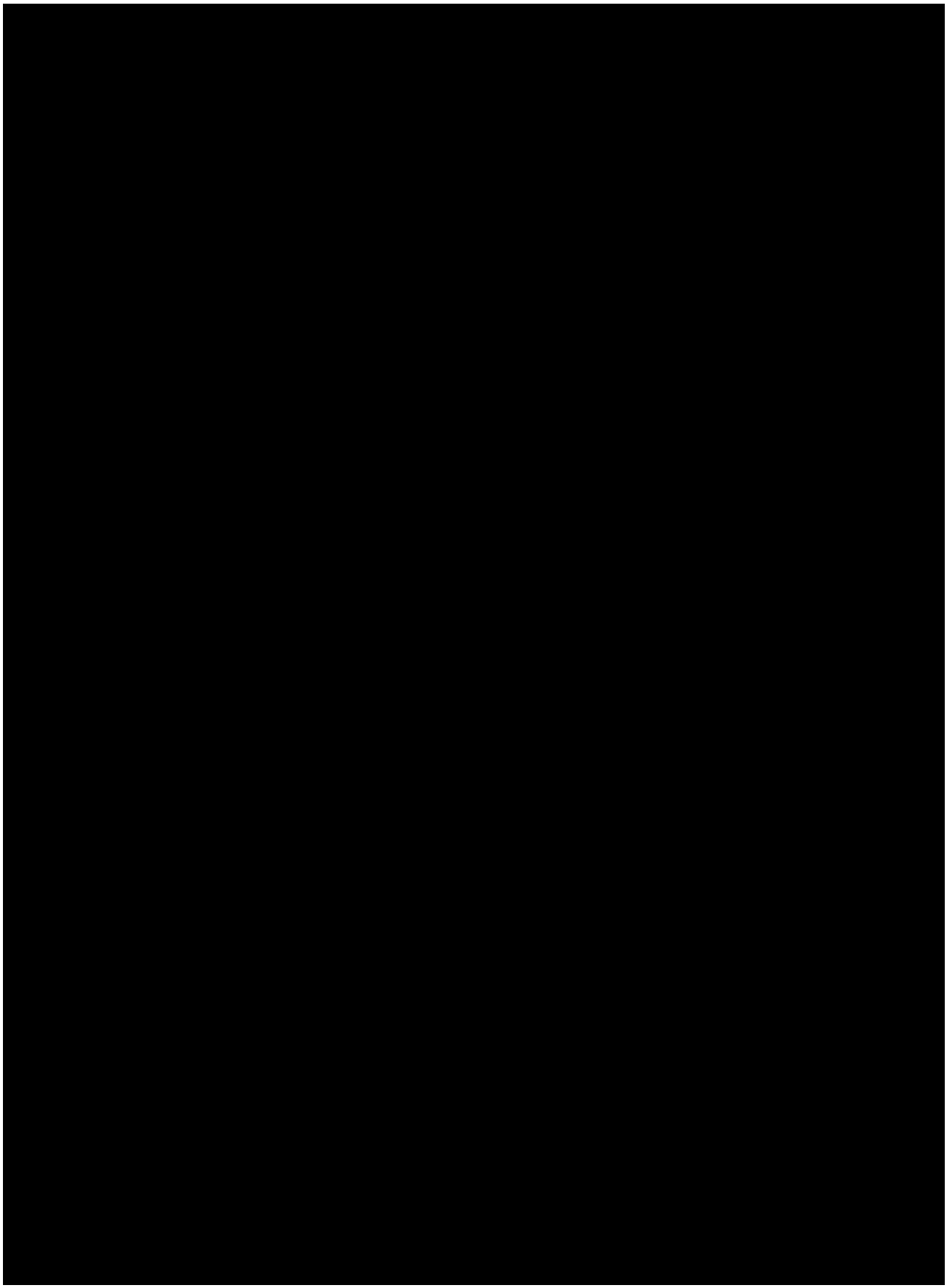

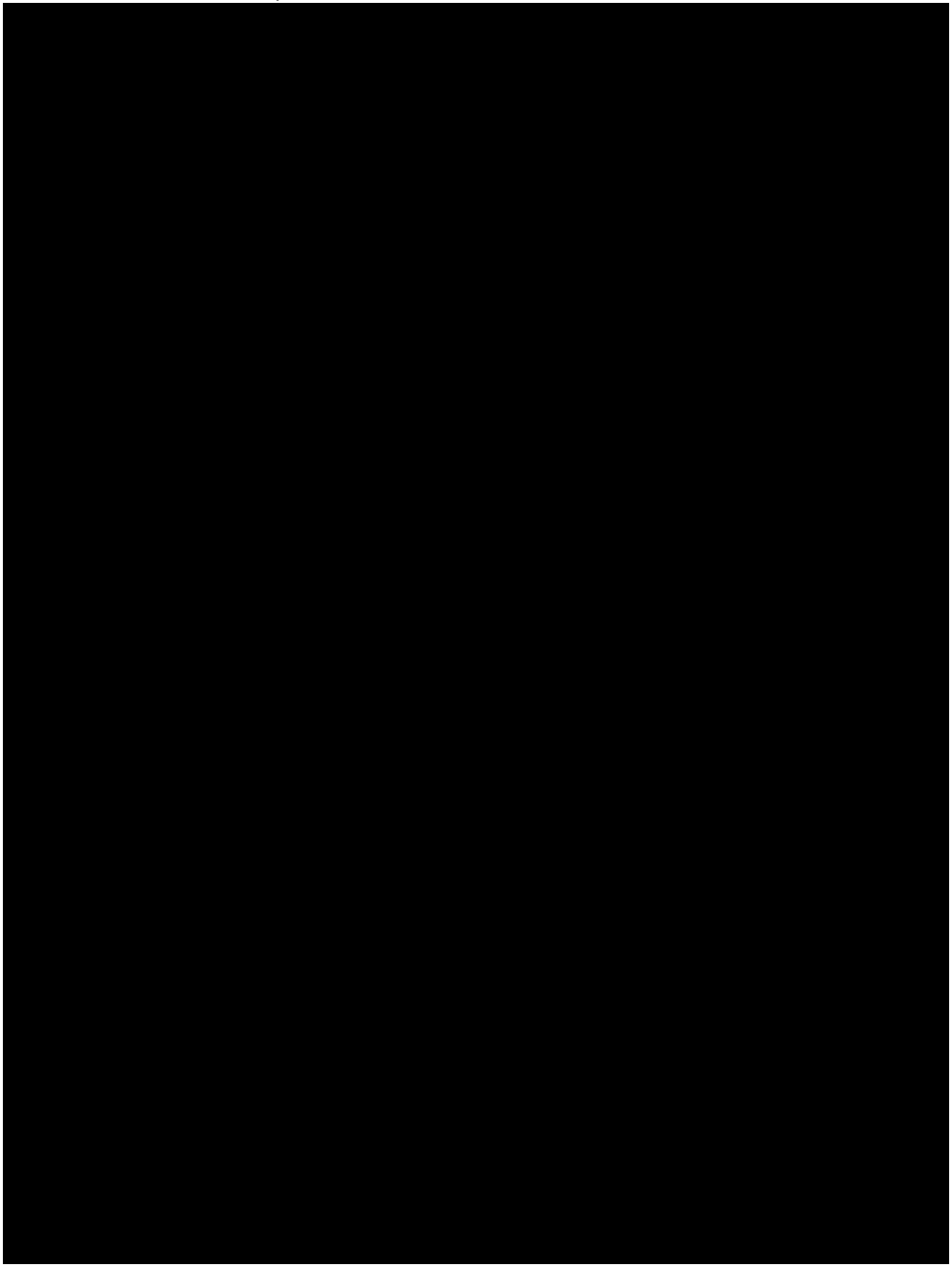

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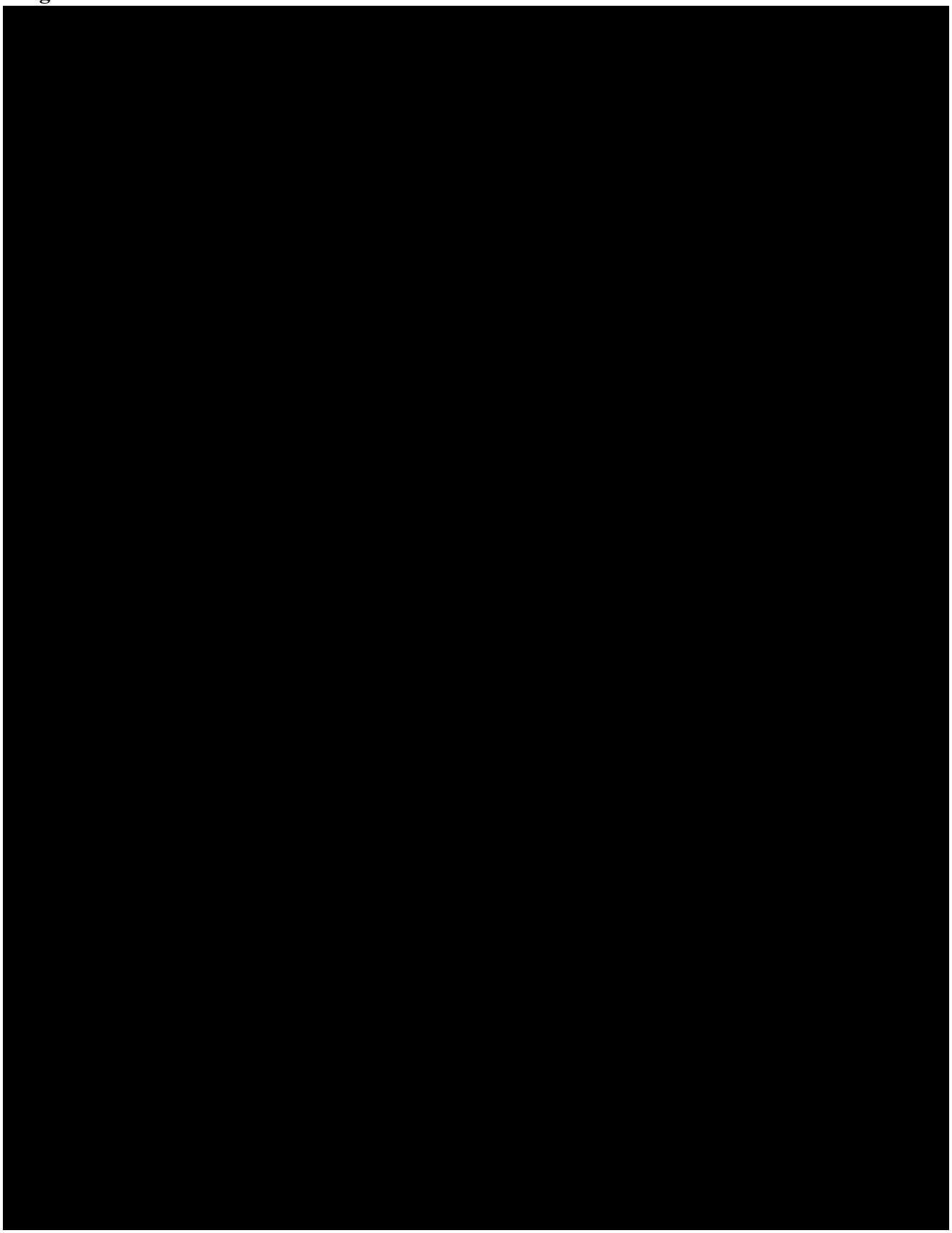
Figures



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