STATISTICAL ANALYSIS PLAN

CLINICAL STUDY PROTOCOL

A Randomized, Double-Masked, Parallel Group, Multicenter, Study to Evaluate Efficacy and Safety of SPARC's SDN-037 Twice Daily Compared with Vehicle for The Treatment of Inflammation and Pain Associated with Ocular Surgery.

Protocol No.	**:** CLR_16_31
Protocol Version	: Version 01 Amendment 03
Protocol Date	**:** 22JAN2020
Plan Version No.	: 1
Plan Version Date	**:** 17SEP2020

STATISTICAL ANALYSIS PLAN

SIGNATURE PAGE

STATISTICAL ANALYSIS PLAN

STATISTICAL ANALYSIS PLAN DETAILS

TRIAL FULL TITLE	A Randomized, Double-Masked, Parallel Group, Multicenter, Study to Evaluate Efficacy and Safety of SPARC's SDN-037 Twice Daily Compared with Vehicle for The Treatment of Inflammation and Pain Associated with Ocular Surgery
CT IDENTIFIER	NCT03426267
SAP VERSION	1
SAP VERSION DATE	17SEP2020
[redacted]	[redacted]
TRIAL CHIEF INVESTIGATOR	MULTI-CENTER
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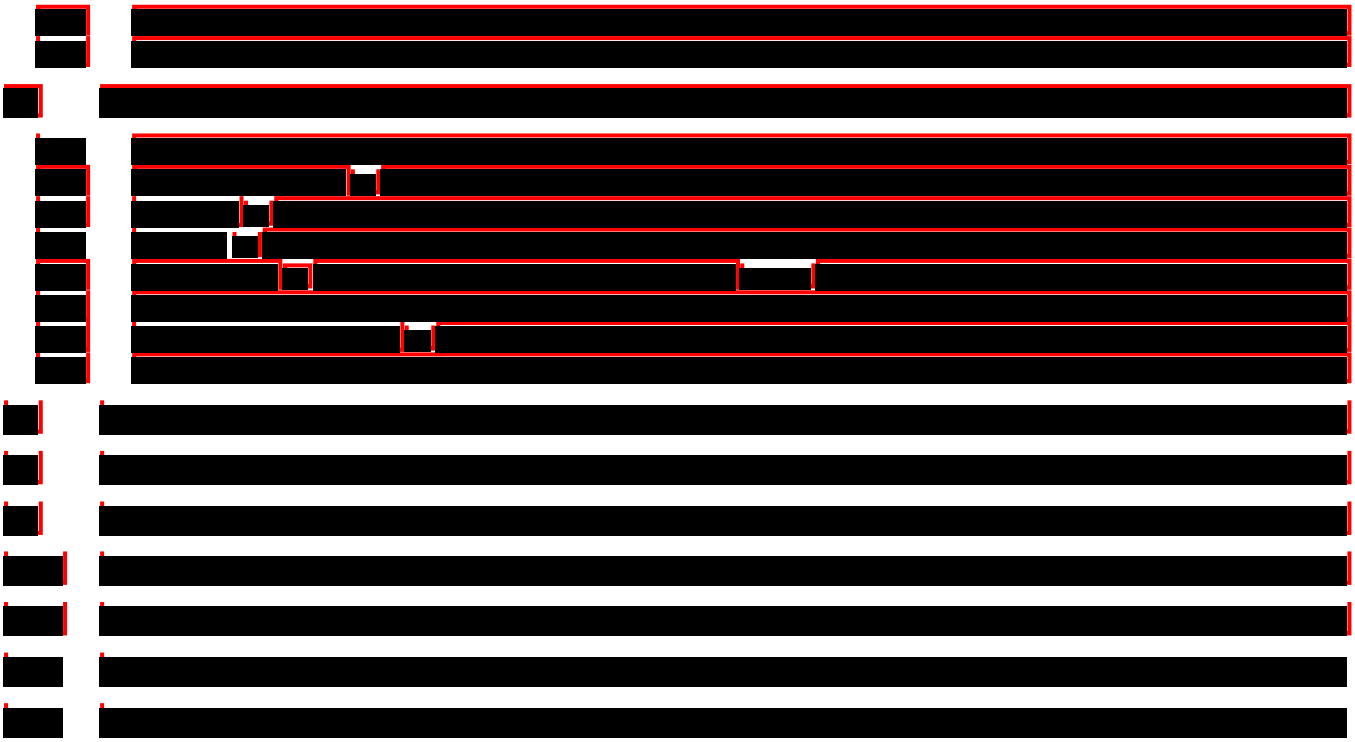
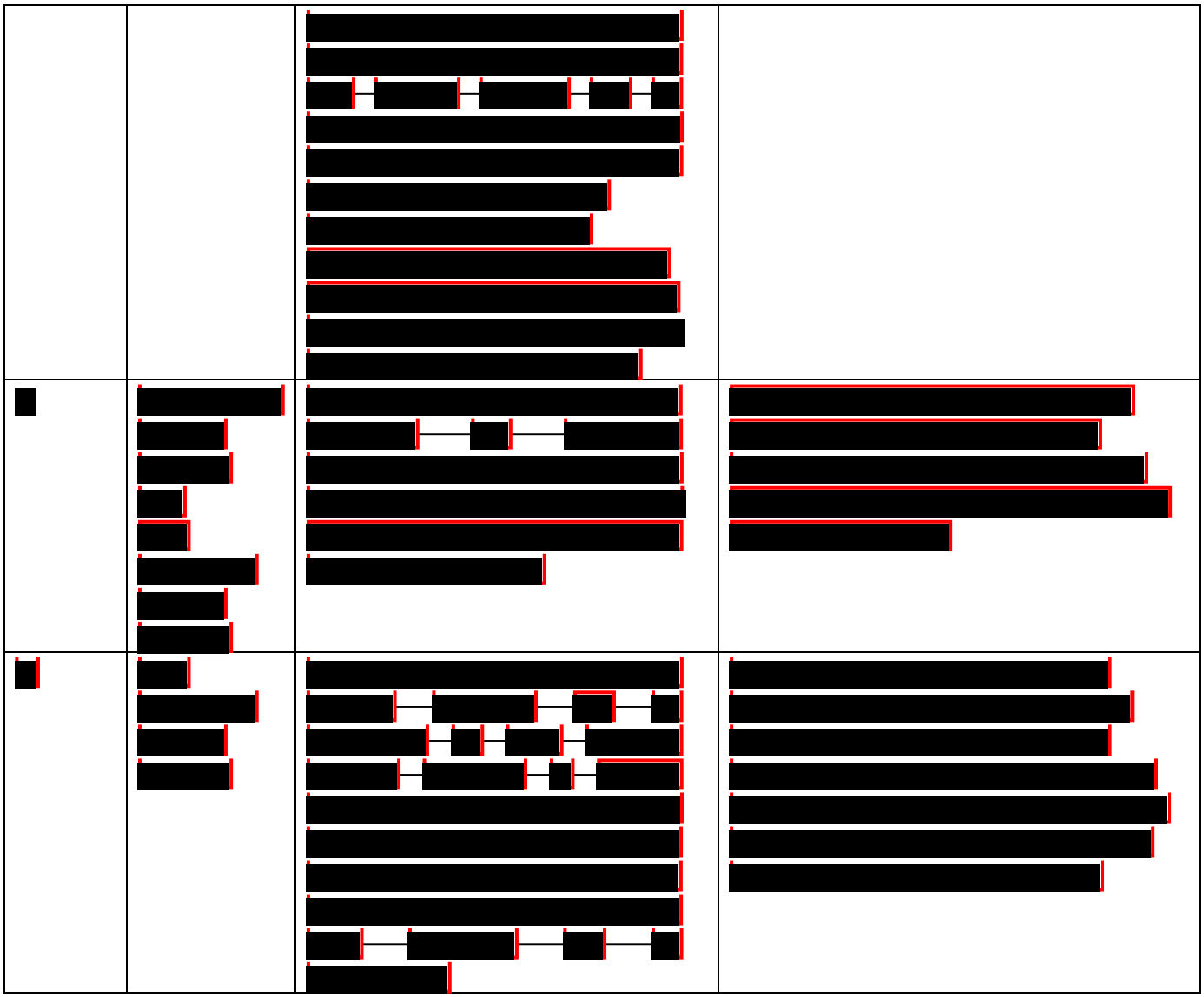


2 ABBREVIATIONS AND DEFINITIONS

ACC	Anterior Chamber Cell
ACF	Anterior Chamber Flare
AE	Adverse Event
BCVA	Best Corrected Visual Acuity
BID	Twice a day (bis in die)
BSCVA	Best-Spectacle Corrected Visual Acuity
CI	Confidence Interval
CRO	Contract Research Organization
eCRF	electronic Case Report Form
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
GLP	Good Laboratory Practice
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	Independent Ethics Committee
IND	Investigational New Drug
IOP	Intraocular Pressure
IOL	Intra Ocular Lens
IP	Investigational Product
IRB	Institutional Review Board
IWRS	Interactive Web Response System
mITT	Modified Intent-To-Treat
LAR	Legally Acceptable Representative
LOCF	Last Observation Carried Forward
logMAR	Logarithm of the Minimum Angle of Resolution
MedDRA	Medical Dictionary for Regulatory Activities
NDA	New Drug Application
OPD	(in-)Office Physician Dispensing
PP	Per Protocol
PT	Preferred Term
RLD	Reference Listed Drug
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SOC	System Organ Class

SPARC	Sun Pharma Advanced Research Company, Ltd.
SUSAR	Suspected Unexpected Serious Adverse Reaction
TEAE	Treatment-Emergent Adverse Event
VAS	Visual Analog Scale
WHO-DD	World Health Organization Drug Dictionary
w/v	Weight/Volume

3 SUMMARY OF LIST OF CHANGES FROM PROTOCOL



4 INTRODUCTION

4.1 Preface

Sun Pharma Advanced Research Company Ltd. (SPARC) has developed a novel topical ophthalmic formulation of difluprednate as a [redacted] for the treatment of inflammation and pain associated with ocular surgery. SPARC intends to develop the ophthalmic difluprednate product at a [redacted] dose [redacted] and with a [redacted], [redacted]

4.2 Purpose of the analyses

These analyses will assess the efficacy and safety of topical administration of [redacted]

5 STUDY OBJECTIVES AND ENDPOINTS

5.1 Study Objectives

To evaluate the efficacy and safety of topical administration of [redacted] dose [redacted] after surgery followed by [redacted].

5.2 Endpoints

Efficacy:

- The primary efficacy endpoint is the proportion of subjects with an ACC grade of 0 at Day 15 [redacted]
- The key secondary efficacy endpoint is the proportion of subjects who achieve a pain score of 0 [redacted] at Day 15.

[redacted]

6 STUDY METHODS

6.1 General Study Design and Plan

- This study is a phase 3, randomized, multicenter, double-masked, vehicle-controlled, parallel-group clinical study.

- **Type of control**: [redacted]
- **Level and method of blinding**: [redacted]
- **Method of treatment assignment**: Subjects who qualify via inclusion and exclusion criteria will be [redacted] assigned to study treatment groups [redacted].
- [redacted]
- [redacted]
- [redacted]

6.2 Inclusion-Exclusion Criteria and General Study Population

- INCLUSION CRITERIA
  1. Be male or female, of 18 years of age or older

     [redacted]
  5. Able to self-instill the IP or have a caregiver available to instill all doses of the IP, as instructed.

6. Females of childbearing potential must not be pregnant (as confirmed by a negative urine pregnancy test [redacted]
7. Be able and willing to follow study instructions and complete all required visits

- EXCLUSION CRITERIA
  1. Any known allergy or hypersensitivity to difluprednate therapy [redacted]
  11. Any active corneal pathology noted in the study eye [redacted]

[redacted]

14. Currently suffering from alcohol and/or drug abuse

[redacted]

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6.4 Study Termination

The study may be stopped at any time by the sponsor, the investigator and/or the IRB with appropriate notification.

If the study is prematurely terminated or suspended for any reason, the investigator/institution should promptly inform the subjects, should assure appropriate therapy and follow-up for the subjects, and, where required by the applicable regulatory requirement(s), should inform the regulatory authority(ies). [redacted]

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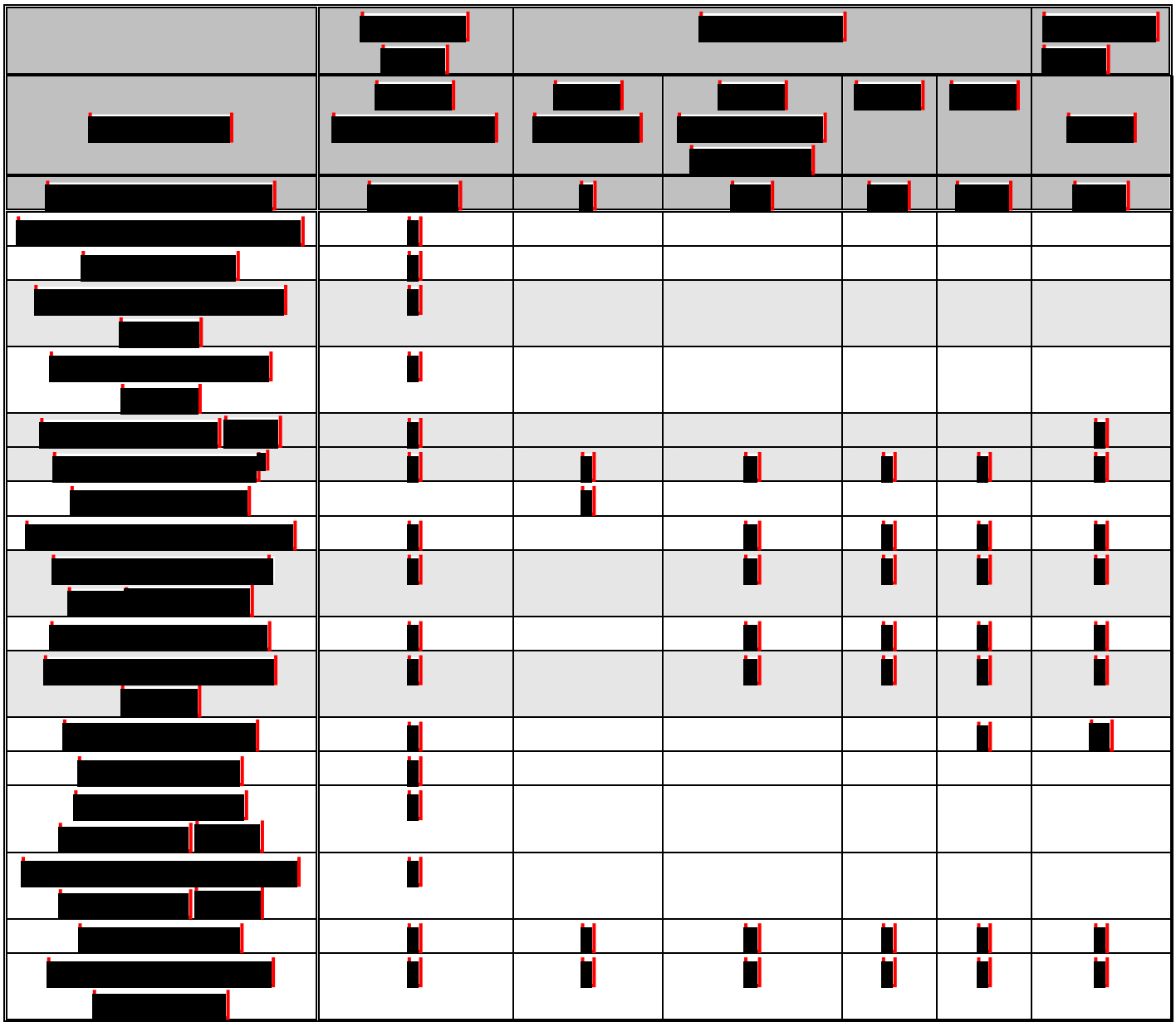

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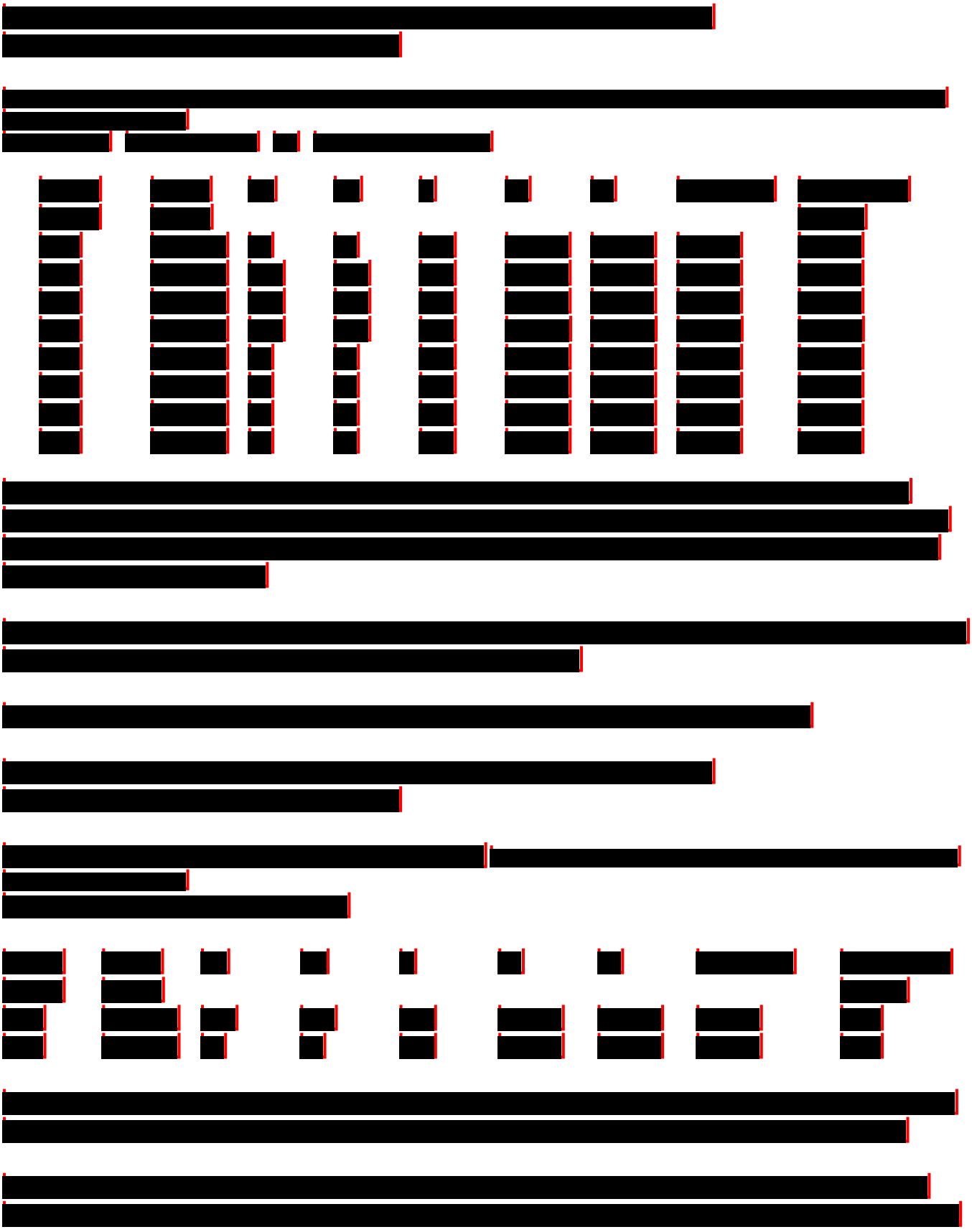

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10 EFFICACY ANALYSIS

10.1 Primary Efficacy Analysis

The primary efficacy endpoint is the proportion of subjects with an ACC grade of 0 at Day 15 [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

11.5 Relationship of Treatment-Emergent Adverse Events to the IP

A summary of TEAEs by SOC, PT, and relationship to the IP will be presented by treatment group. The relationships indicate the investigator's assessment of whether or not the event was caused by the IP. The possible relationships are "Unrelated", "Unlikely", "Possibly", "Probably", and "Certainly".[redacted]

[redacted]

11.6 Serious Adverse Events

Serious adverse events (SAEs) will be listed by subject; SAEs will be summarized by event and treatment group.

11.7 Adverse Events Leading to Study Drug Withdrawal

All AEs leading to study withdrawal or study drug withdrawal will be listed and summarized.

[redacted]

[redacted]

12 REPORTING CONVENTIONS

Summary tables and listings (e.g., post text tables and individual subject data listings are prepared according to ICH Guideline E3) include a header, showing Protocol Number, Status, and sponsor; and a "footer" providing explanatory notes that indicate as a minimum:

- SAS program name and data file source
- Date of data extraction
- Date of output generation

Post text tables also include reference(s) to the subject data listing(s) that supports the summary data. The data extraction date links the output to the archived database that is locked to ensure the replication of the results.

Post text tables will be organized with respect to treatment groups for safety and efficacy. The order of presentation will be chronological for visits. A total column will appear as the last column, as applicable. The summary tables clearly indicate the number of subjects to which the data apply and unknown or not performed are distinguished from missing data.

Summary tables for medications and medical conditions are coded according the WHO Drug Dictionary and MedDRA respectively. Adverse event preferred terms and body/organ systems are coded using the MedDRA dictionary. The MedDRA dictionary can be used, as well, in the coding of signs and symptoms, medical history, physical examination abnormalities, and clinical diagnoses.

Supportive individual subject data listings, at a minimum, are sorted and presented by subject ID and treatment. Listings also include visit number, visit date, and days relative to the initiation of treatment.

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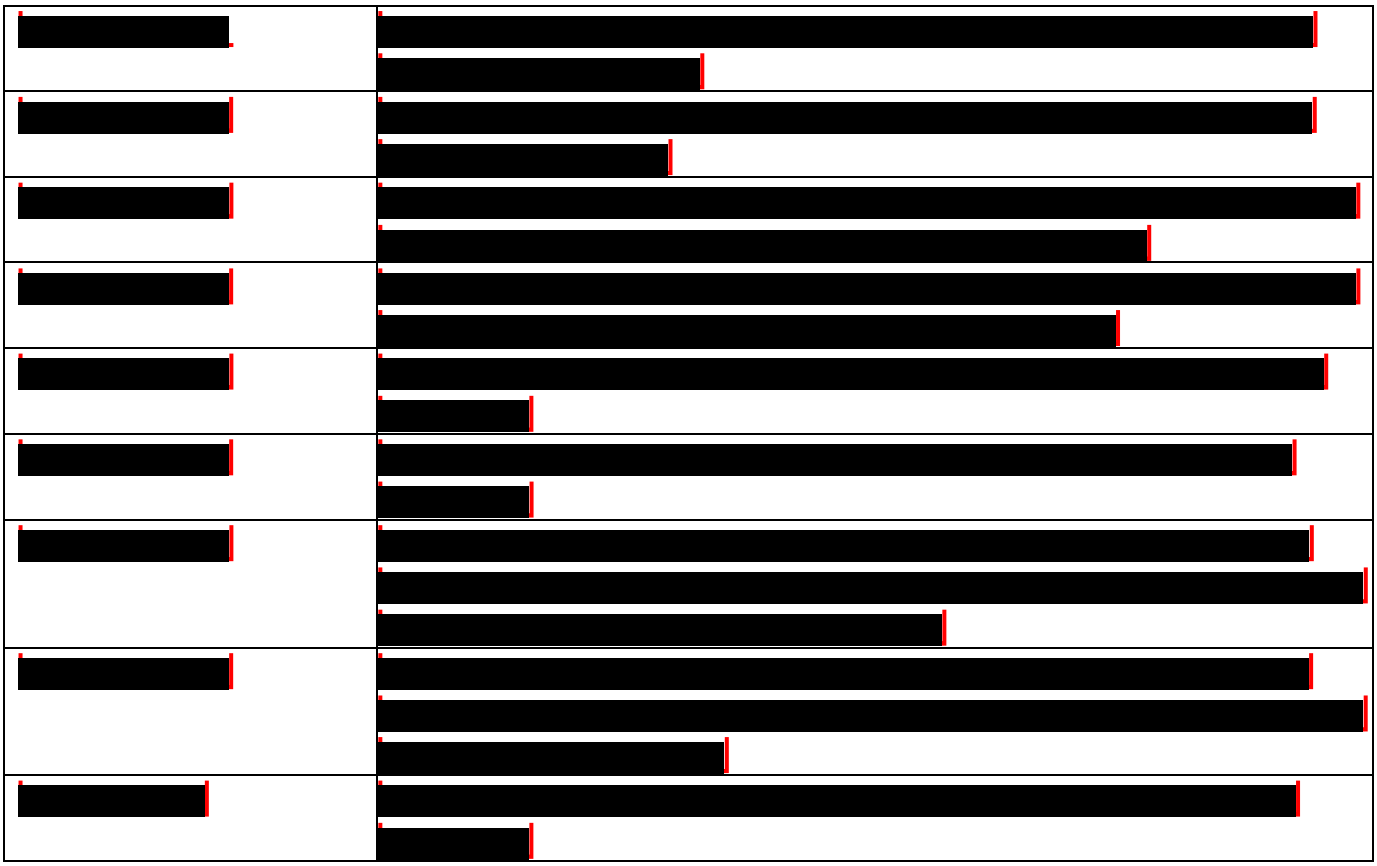

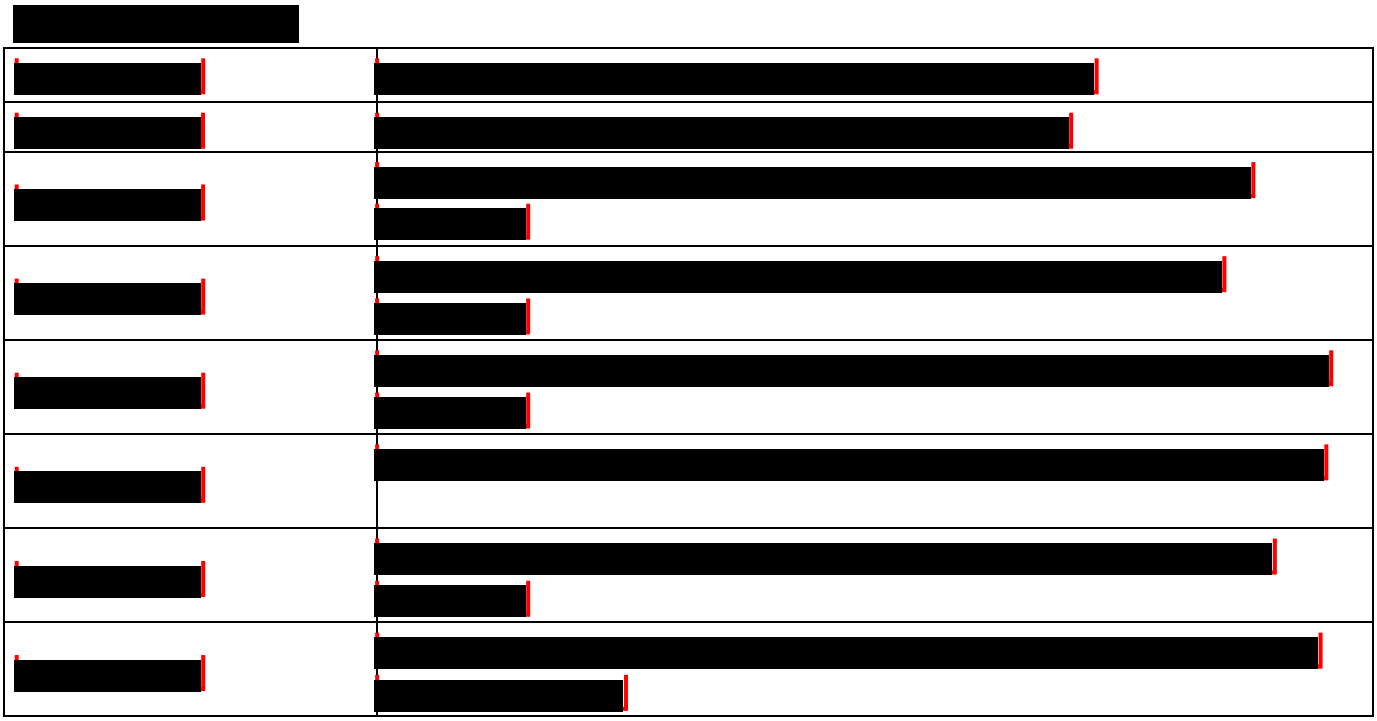

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