STATISTICAL ANALYSIS PLAN
PHASE II

VERSION: 2.0
DATE OF PLAN:

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BASED ON:

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STUDY DRUG:

DFD-03 Lotion

PROTOCOL NUMBER:

DFD-03-CD-008

STUDY TITLE:

A Randomized, Double-Blind, Active-Controlled Study to Assess the Safety and Local Tolerability of DFD-03 (tazarotene) Lotion, 0.1% compared to Tazorac® (tazarotene) Cream, 0.1% in the Topical Treatment of Acne Vulgaris for 12 Weeks

SPONSOR:

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This study is being conducted in compliance with good clinical practice, including the archiving of essential documents.

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TECHNICAL SUMMARY REPORT (TSR)

Name of Sponsor/Company Dr. Reddy's Laboratories, Ltd	**Individual Study Table Referring to Part of the Dossier:** **Volume:**	***(For National Authority Use Only)*:**
Name of Finished Product: DFD-03 Lotion	**Page:**	
Name of Active Ingredient: Tazarotene		
Title Of Study: A Randomized, Double-Blind, Active-Controlled Study to Assess the Safety and Local Tolerability of DFD-03 (tazarotene) Lotion, 0.1% compared to Tazorac® (tazarotene) Cream, 0.1% in the Topical Treatment of Acne Vulgaris for 12 Weeks		
Investigators: Study Centers: 10		
Studied period (weeks): 12	**Phase of development:** II	
Objective: The objectives of this study were to determine the safety and local tolerability of DFD-03 (tazarotene) Lotion 0.1% and to compare it with Tazorac (tazarotene) Cream, 0.1% in the topical treatment of acne vulgaris for 12 weeks.		
Methods: This was a multicenter, randomized, double-blind, parallel-group, active-controlled study. Subjects with mild to moderate facial acne vulgaris were randomized to treatment with either DFD-03 (tazarotene) Lotion 0.1%, Tazorac (tazarotene) Cream, 0.1%, Vehicle Lotion or Vehicle Cream in a ratio of 2:2:1:1. Upon randomization, the treatment group (DFD-03 group or Tazorac group) were known but the treatment assignment (active vs. vehicle) within that treatment group remained blinded. During the 12-week treatment period subjects randomized to DFD-03 Lotion or Vehicle Lotion used the study drug twice daily with approximately 12 hours between applications. Subjects randomized to Tazorac Cream or Vehicle Cream used the study drug once daily in the evening. Subjects will be instructed to treat the entire face. At selected site(s), subjects with acne lesions of any severity on the chest and/or back (including shoulders) were enrolled provided they have met all inclusion criteria including mild to moderate acne on the face and have not met any exclusion criteria and will treat all areas affected with acne on the face, chest and/or back, including shoulders, if applicable. Up to 12 subjects with acne involvement on the face, chest and/or back including shoulders were randomized to treatment with either DFD-03 (tazarotene) Lotion 0.1%, Tazorac (tazarotene) Cream, 0.1%, Vehicle Lotion or Vehicle Cream in a ratio of 2:2:1:1. At selected site(s), subjects who are 9 to 11 years of age were randomized to DFD-03 group only in a 1:1 ratio of DFD-03 (tazarotene) Lotion 0.1% to Vehicle Lotion. Approximately 8 subjects were enrolled in this age range and the inclusion criteria on the number of inflammatory and non-inflammatory lesions was not be applicable to these subjects. Safety assessments included the investigator's assessment of local cutaneous tolerance/application site reactions on the face (dryness, non-lesional erythema, peeling, stinging, burning, and itching), vital signs (blood pressure and pulse rate), and adverse events (AEs). Local cutaneous tolerance reactions on the chest and/or back including shoulders (if applicable), were assessed separately. Urine pregnancy tests were performed at Screening, Baseline and at every visit through Week 12 for all female subjects. A physical examination was performed at the Baseline and at the End of Study Visit.		

The Cardiff Acne Disability Index (CADI) was used to assess the quality of life in all subjects at Baseline (Day 1) and at Weeks 4, 8 and 12.

The investigator assessed efficacy by using an Investigator's Global Assessment scale (IGA 5-point scale) and by counting the number of inflammatory and non-inflammatory lesions on the face at Baseline and Weeks 4, 8, and 12.

Number of Subjects:

Approximately 150 subjects with facial acne vulgaris were randomized at 10 centers to ensure at least 120 subjects will complete the study.

Diagnosis and Criteria for Inclusion / Exclusion (see protocol section 5.1 and 5.2):

Inclusion Criteria:

1. Subject understood the study procedures, was willing to comply with the study procedures and required visits, and agreed to participate by giving written informed consent. Subjects under the legal age of consent provided written assent and had the written informed consent of their legal guardian.
2. Subject (or legal guardian) was willing to authorize use and disclosure of protected health information collected for the study.
3. Subject was at least 12 years of age.
    a. At selected site(s), a total of approximately eight subjects 9-11 years of age were enrolled into the 2 arms of DFD-03 lotion group (active and vehicle).
4. Female subjects were required to have their menstrual period at the Baseline Visit (as reported by the subject), except for subjects using hormonal contraceptives that preclude menstrual periods, if the subject was premenarchal, was postmenopausal for at least 12 months prior to baseline, was surgically sterilized (i.e. tubal ligation) or if the subject was without a uterus and/or both ovaries.
5. A clinical diagnosis of facial acne vulgaris with a facial Investigator's Global Assessment (IGA) score of 2 (mild) to 3 (moderate) at Baseline.
    a. At selected site(s), up to twelve subjects with acne lesions on the chest and/or back (including shoulders) in addition to those on the face had the option of treating their back and/or chest (including shoulders) in addition to their face.
6. Inflammatory lesion count (papules and pustules) of at least 20 on the face, including the nose, at Baseline.
    a. This criteria was not applicable to the 9-11 years age group as long as subjects had an IGA score of 2 (mild) to 3 (moderate) at Baseline.
7. Non-inflammatory lesion count (closed and open comedones) of at least 25 on the face, including the nose, at Baseline.
    a. This criteria was not applicable to the 9-11 years age group as long as subjects had an IGA score of 2 (mild) to 3 (moderate) at Baseline.
8. No more than 2 nodulocystic lesions on the face, including the nose, at Baseline.
9. Females, regardless of childbearing potential:
    a. Must have had a negative urine pregnancy test at Screening and Baseline. Test must have had a sensitivity of at least 25 mIU/mL for βhCG.
    b. If sexually active, must have been on or used an acceptable method of birth control. Acceptable methods of birth control included:
        - hormonal methods* or intrauterine device in use ≥ 90 days prior to Baseline; or
        - partner has had a vasectomy at least 90 days prior to Baseline; or

- barrier methods plus spermicide; or
- Essure® that had been in place for at least 3 months before the screening visit with radiograph confirmation of fallopian tube blockage.

***Hormonal methods:** If on hormonal contraceptives, must have been on the same hormonal contraceptive product for 3 months (90 days) prior to Baseline and continued on the same method and dose throughout the duration of the study. If subject had used hormonal birth control and had stopped, this should have occurred more than 6 months prior to Baseline.

Exception: Sexually inactive female subjects were not required to practice a reliable method of contraception and were enrolled at the investigator's discretion provided that they were counseled to remain sexually inactive for the duration of the study and understood the possible risks involved in getting pregnant during the study. An abstinent female must have agreed that if she became sexually active during the study she would use an acceptable form of contraception such as a barrier method with spermicide. Females who are surgically sterilized [e.g. hysterectomy, bilateral tubal ligation, bilateral oophorectomy] at least 1 year prior to Baseline or have been postmenopausal for at least 1 year prior to Baseline are not required to practice a reliable method of contraception.

10. Subjects agreed not to use any product on the face during the entire course of study except for non-medicated, investigator-approved cleanser, sunscreen, face wash, and make-up. Subjects should have continued to use these investigator-approved products for the duration of the study and should avoid any changes in these consumer products.
11. Subjects were willing to comply with sun avoidance measures for the face (as well as back/chest and shoulders, if applicable) including use of investigator-approved sunscreen and/or hats, had limited sun exposure time, and had no tanning bed use.
12. Subject must have been in good general health as determined by the investigator and supported by the medical history, physical examination, and normal or not clinically significant abnormal vital signs (blood pressure and pulse). Subjects were eligible if:
    a. Systolic blood pressure (BP) < 160 and > 85 mmHg
    b. Diastolic BP < 100 and > 50 mmHg
    c. Pulse 50 to 100 bpm inclusive for adults; up to 110 bpm for subjects < 18 years of age

Exclusion Criteria:

1. Females who were pregnant or lactating or planning to become pregnant during the study period.
2. Treatment with the following products:
    a. Topical acne treatments (retinoids, antibiotics, benzoyl peroxide, azelaic acid, resorcinol, salicylates, α-hydroxy/glycolic acid), or other topical facial medication (antifungals, steroids, anti-inflammatories) on the treatment area in the 14 days prior to the Baseline Visit, including prescription and non-prescription products.
    b. Systemic corticosteroids, systemic acne treatments including systemic antibiotics used for treatment of acne, potential photosensitizing agents (thiazides, phenothiazines), spironolactone, flutamide, or immunosuppressant drugs in the 30 days prior to the Baseline Visit.
    c. Systemic retinoid use (including high dose vitamin A > 10,000 units per day) in the 180 days prior to the Baseline Visit.
    d. Undertaken certain facial procedures such as chemical peel, laser treatment, photodynamic therapy, acne surgery, cryodestruction or chemodestruction, x-ray therapy, intralesional steroids, dermabrasion, or depilation (except eyebrow shaping) in the 30 days prior to the

Baseline Visit. After the subject is enrolled in the study, eyebrow shaping (except for tweezing) is prohibited.

e. Treatment with a medication or procedure that, in the opinion of the investigator, would put the subject at unacceptable risk for participation in the study or may interfere with evaluations in the study.

f. Treatment with an investigational product or device in the 30 days prior to the Baseline Visit.

3. Known allergic reaction to retinoids or tazarotene or any of the other ingredients of these products. The inactive ingredients are sodium lauryl sulphate, stearyl alcohol, cetyl alcohol, gluconolactone, Vitamin E polyethylene glycol succinate, glycerin, carbomer P 971, propylparaben, methylparaben, edetate disodium, butylated hydroxytoluene, medium-chain triglyceride, trolamine, and purified water.
4. Presence of any facial skin disease or condition that would interfere with the study or place the subject at unacceptable risk including sunburn, rosacea, seborrheic dermatitis, perioral dermatitis, lupus, dermatomyositis, psoriasis, eczema, squamous cell carcinoma, acneiform eruptions caused by medications, steroid acne, steroid folliculitis, bacterial folliculitis or any other facial disease or condition.
5. Excessive facial hair (i.e., heavy beard or mustache), facial tattoos or facial disfigurement that would interfere with study assessments.
6. Subjects with a serious and/or chronic medical condition such as chronic or active liver disease, renal impairment, heart disease, severe respiratory disease, rheumatoid arthritis, current malignancies, immunocompromised conditions, or any other disease that, in the opinion of the investigator, would interfere with the study or place the subject at unacceptable risk.
7. Subjects who have been treated for alcohol dependence or alcohol or drug abuse in the year prior to the Baseline Visit.
8. Subjects who have been in another investigational trial within 30 days of the Baseline Visit.
9. Subjects were not to have a personal relationship with any member of the study staff or be part of the staff at the medical practice.

Investigational Product, Dose and Mode of Administration:

DFD-03 Lotion (0.1% tazarotene) or Vehicle Lotion

Subjects were to apply a quarter (U.S coin) size amount of the study product all over the moistened face and rub it into the skin until foamy. Care should have been taken to avoid the areas around the eyes, mouth, and nostrils. After being left on for 1 minute, the subject was to rinse off the product by thoroughly rinsing with warm water for about 30 seconds. This procedure was to be followed twice daily, in the morning and at bedtime, approximately 12 hours apart.

For those subjects treating chest and/or back, including shoulders at selected site(s), an additional 1-2 quarter size amount of the study product was to be used over other affected areas and applied similarly as on the face.

Duration of Treatment and Study:

Subjects were to treat the entire face, including the nose (and only at selected site(s), chest and/or back, including shoulders) twice daily for 12 weeks. The total study duration including the screening period was approximately 12 to 20 weeks.

Reference and Control Products, Dose and Mode of Administration:

Tazorac (tazarotene) Cream, 0.1% or Vehicle Cream

Approximately 1 g (pea size amount) of investigational product was applied over the entire face once daily at bedtime and left on overnight.

At selected site(s), an additional amount of 1-2 g investigational product was applied to chest and/or back (including shoulders), if applicable and left overnight.

Criteria for Evaluation (see protocol section 11):

Safety Criteria:

Safety endpoints included local tolerability/application site reaction occurrence and adverse events. Comparison of local tolerability and safety of DFD-03 Lotion with Tazorac Cream was the primary endpoint for this study.

Local tolerability/application site reactions included dryness, non-lesional erythema, peeling, stinging/burning, and pruritus and were assessed at each study visit from Baseline through End of Study. The reactions on the face were assessed separately from those on the chest and/or back, including shoulders (if applicable). Other safety variables included physical examination and vital signs (blood pressure and pulse rate).

Efficacy Criteria:

The following efficacy endpoints will be summarized using descriptive statistics for both the ITT and PP populations:

- Proportion of Subjects with IGA Success at Weeks 4, 8 and 12. IGA success is defined as an IGA score of 0 (Clear) or 1 (Almost Clear) with at least a 2-grade reduction from baseline.
- Absolute Change from Baseline in Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Absolute Change from Baseline in Non-Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Percent Change from Baseline in Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Percent Change from Baseline in Non-Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Change from Baseline to Weeks 4, 8 and 12 in CADI.

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1. LIST OF ABBREVIATIONS

Table 1: List of Abbreviations

Abbreviation	Term
AE	Adverse Event
BP	Blood Pressure
CADI	Cardiff Acne Disability Index
CRF	Case Report Form
CSR	Clinical Study Report
DRL	Dr. Reddy's Laboratories
FDA	Food and Drug Administration
IGA	Investigator's Global Assessment
ITT	Intent-to-Treat Population
IWRS	Interactive Web-Based Response System
LOCF	Last Observation Carried Forward
MedDRA	Medical Dictionary for Regulatory Activities Terminology
n	Observed Sample Size
N	Total Sample Size
PCS	Potentially Clinically Significant
PP	Per-Protocol Population
PT	Preferred Term
SAE	Serious Adverse Event
SAS	Statistical Analysis System
SD	Standard Deviation
SOC	System Organ Class
TEAE	Treatment-Emergent Adverse Event
TEAESI	Treatment Emergent Adverse Event of Special Interest
TESAE	Treatment-Emergent Serious Adverse Event
TSR	Technical Summary Report
WHO	World Health Organization
WHODD	World Health Organization Drug Dictionary

2. INTRODUCTION

The purpose of this statistical analysis plan (SAP) is to describe the planned analyses and data displays to be included in the Clinical Study Report (CSR) for Protocol DFD-03-CD-008.

Protocol Revision Chronology:		
Protocol	02-JUN-2017	Original
Amendment 01	06-NOV-2017	Amendment No. 01: This protocol amendment was implemented based on recommendations from the FDA and includes the following: 1. To update Inclusion Criteria #3 to include subjects 9 to 11 years of age that will be enrolled at selected site(s) and to clarify that efforts will be made to include approximately 8 subjects in the 9-11 years age group in the 2 arms of DFD-03 lotion (active and vehicle included) where a treatment assignment schedule will be created with kit numbers randomly assigned to study products which is independent from the treatment assignment schedule created for ages 12 years and older. 2. To update Inclusion Criteria #5 to specify that at selected sites(s), subjects with acne lesions on the chest and/or back (including shoulders) in addition to those on the face will treat these affected areas and to specify that up to 12 subjects with acne involvement on the face, chest and/or back including shoulders will be randomized to treatment with either DFD-03 (tazarotene) Lotion 0.1%, Tazorac (tazarotene) Cream, 0.1%, Vehicle Lotion or Vehicle Cream in a ratio of 2:2:1:1. 3. To update Inclusion Criteria #6 to specify there is no required inflammatory lesion count for subjects 9-11 years of age. 4. To update Inclusion Criteria #7 to specify there is no required non-inflammatory lesion count for subjects 9-11 years of age. 5. To update Inclusion Criteria #9 to clarify that women who are surgically sterilized (e.g. hysterectomy, bilateral tubal ligation, bilateral oophorectomy) at least 1 year prior to baseline or have been postmenopausal for at least 1 year prior to baseline, do not have to practice birth control measures. 6. To clarify that if acne lesions are present on the chest and/or back (including shoulders), that these lesions will be counted and recorded separately at each visit from Baseline to Week 12 and local cutaneous tolerance evaluation will be assessed and recorded separately. 7. To clarify restriction on who may be involved with the dispensing or return of study medication. In addition, minor administrative changes were made to correct grammar, formatting, and punctuation to ensure consistency, including the following: • to update the Sponsor's contact person

This SAP was developed in accordance with ICH E9 guideline. All decisions regarding final analysis, as defined in this SAP document, will be made prior to Database Freeze (unblinding) of the study data. Further information can be found in the protocol.

The statistical analysis plan (SAP) is based on:

- Protocol No. DFD-03-CD-008, Version 2.0, Amendment 01, dated 06-NOV-2017
- ICH guidelines E4 and E9 (Statistical Principles for Clinical Trials)
- Discussions with the FDA

The purpose of this document is to provide details on study populations and on how the variables will be derived, how missing data will be handled as well as details on statistical methods to be used to analyze the safety and efficacy data for Study Protocol No. DFD-03-CD-008.

The document may evolve over time, for example, to reflect the requirements of protocol amendments or regulatory requests. However, the final SAP must be finalized, approved by the Sponsor, and placed on file before database is locked. Deviations from the final approved plan will be noted in the clinical study report.

3. STUDY OBJECTIVES AND ENDPOINTS

3.1. Study Objectives

The objectives of this study were to determine the safety and local tolerability of DFD-03 (tazarotene) Lotion 0.1% and to compare it with Tazorac (tazarotene) 0.1% Cream in the topical treatment of acne vulgaris for 12 weeks.

3.2. Study Endpoints

3.2.1. Primary Endpoints

The primary safety endpoints are:

- Local Cutaneous Safety Evaluation Data (dryness, non-lesional erythema, peeling, stinging, burning, and itching). Reactions on the face were assessed separately from those on the chest/back/shoulders.
- Treatment-Emergent Adverse Events (TEAEs).

3.2.2. Secondary Endpoints

The secondary safety endpoints are:

- Vital Signs (blood pressure and pulse rate)
- Physical Examination Data

The secondary efficacy endpoints are:

- Proportion of Subjects with IGA Success at Weeks 4, 8 and 12. IGA success is defined as an IGA score of 0 (Clear) or 1 (Almost Clear) with at least a 2-grade reduction from baseline.
- Absolute Change from Baseline in Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Absolute Change from Baseline in Non-Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Percent Change from Baseline in Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Percent Change from Baseline in Non-Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Change from Baseline in Cardiff Acne Disability Index (CADI) at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.

4. STUDY DESIGN

4.1. Summary of Study Design

This was a multicenter, randomized, double-blind, parallel-group, active-controlled study. Approximately 150 subjects with mild to moderate facial acne vulgaris were randomized in a 2:2:1:1 ratio to treatment with DFD-03 (tazarotene) Lotion 0.1%, Tazorac (tazarotene) Cream, 0.1%, Vehicle Lotion, or Vehicle Cream. During the 12-week treatment period subjects randomized to DFD-03 Lotion or Vehicle Lotion used the study drug twice daily with approximately 12 hours between applications. Subjects randomized to Tazorac Cream or Vehicle Cream used the study drug once daily in the evening.

At selected site(s), subjects with acne lesions of any severity on the chest and/or back (including shoulders) may have been enrolled provided they have met all inclusion criteria including mild to moderate acne on the face and have not met any exclusion criteria and treated all areas affected with acne on the face, chest and/or back, including shoulders, if applicable. Up to 12 subjects with acne involvement on the face, chest and/or back including shoulders were randomized to treatment with either DFD-03 (tazarotene) Lotion 0.1%, Tazorac (tazarotene) Cream, 0.1%, Vehicle Lotion or Vehicle Cream in a ratio of 2:2:1:1.

Also, there were selected site(s) that enrolled approximately 8 subjects who are 9 years of age to 11 years of age. They were randomized to DFD-03 group only in a 1:1 ratio of DFD-03 (tazarotene) Lotion 0.1% to Vehicle Lotion. The total number of approximately 150 subjects in the study included up to 12 subjects with acne on the chest and/or back, and approximately 8 subjects in the age group of 9-11 years.

4.2. Definition of Study Drugs

The study drugs were:

- DFD-03 (tazarotene) Lotion 0.1% (60 mL bottle containing 50 ml of study product, Dr. Reddy's Laboratories Ltd.)
- Vehicle Lotion (0% tazarotene) (60 mL bottle containing 50 ml of study product, Dr. Reddy's Laboratories Ltd.)
- Tazorac (tazarotene) 0.1% Cream (60-gram tube, Allergan, Inc.)
- Vehicle Cream (0% tazarotene) (60-gram tube, Dr. Reddy's Laboratories Ltd.)

The study products were provided by Dr. Reddy's Laboratories Ltd., Hyderabad, India. The study products were white to off-white lotions and white to off-white creams. The ingredients of the Vehicle Lotion and Vehicle Cream were identical to DFD-03 Lotion and Tazorac Cream, respectively, except for omission of tazarotene.

4.3. Sample Size Considerations

The sample size was not powered to obtain statistical significance, but was expected to provide an estimate on comparability of local tolerability/safety of DFD-03 versus Tazorac Cream and their respective Vehicles.

4.4. Randomization

Subjects were assigned randomly to one of the four treatment arms, DFD-03 (tazarotene) Lotion 0.1%, Tazorac (tazarotene) Cream, 0.1%, Vehicle Lotion or Vehicle Cream in a 2:2:1:1 ratio (50 subjects each to DFD-03 Lotion and Tazorac Cream, and 25 subjects each to Vehicle Lotion and Vehicle Cream). A treatment assignment schedule was created with kit numbers randomly assigned to study products. The date and time of randomization and the bottle/tube number should have been entered on the eCRF.

For the selected site(s) enrolling subjects in the 9-11 age group, subjects were assigned randomly to one of the two treatment arms, DFD-03 (tazarotene) Lotion 0.1%, and 0.1%, Vehicle Lotion in a 1:1 ratio (4 subjects each to DFD-03 Lotion and Vehicle Lotion). A treatment assignment schedule was created with kit numbers randomly assigned to study products, which is independent from the treatment assignment schedule created for ages 12 and older.

For the selected site(s) enrolling subjects with acne involvement on the face, chest and/or back including shoulders, subjects were assigned randomly to treatment with either DFD-03 (tazarotene) Lotion 0.1%, Tazorac (tazarotene) Cream, 0.1%, Vehicle Lotion or Vehicle Cream in a 2:2:1:1 ratio. Since these subjects were treating their face, chest and/or back and shoulders, the subject kit size contained more study medication for application. A treatment assignment schedule was created for these larger kit sizes with kit numbers randomly assigned to study products, which is independent from the treatment assignment schedules created for ages 9-11 and 12 and older.

A unique subject number was assigned to each subject. The randomization number (kit number) was designated as the subject number. The subject maintained the same subject number and treatment assignment throughout the study. Subject numbers were assigned immediately prior to dispensing study medication and were assigned starting with the lowest available number at the study site.

The Investigator designated an independent third party study medication dispenser who dispensed to qualified subjects, collected all bottles/tubes of study product and dispensed and collected diaries.

No stratification based on age or other characteristics was performed.

4.5. Clinical Assessments

Clinical assessments are summarized in Table 2.

Table 2: Study Schedule

	Visit 1	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**
	Screen[1] Day -60 to 0	**Day 1[1] Baseline**	**Week 4[2] Day 28**	**Week 8[3] Day 56**	**Week 12[3] Day 84**
Informed Consent/assent	X				
Inclusion and exclusion criteria	X	X			
Medical (including acne) history / prior and concomitant medications	X	X			
Collect Demographic Data	X				
Fitzpatrick Skin Type Assessment		X			
Physical Examination (including height and weight at Baseline Visit only)		X			X
Vital signs assessment (Blood Pressure and Pulse Rate)	X	X	X	X	X
Update concomitant medication			X	X	X
Urine pregnancy test[4]	X	X	X	X	X
Randomization		X			
Dispense/redispense study product		X	X	X	

	Visit 1	**Visit 2**	**Visit 3**	**Visit 4**	**Visit 5**
	Screen[1] **Day -60 to 0**	**Day 1**[1] **Baseline**	**Week 4**[2] **Day 28**	**Week 8**[3] **Day 56**	**Week 12**[3] **Day 84**
Weigh study product bottles prior to dispensing and used bottles upon return		X	X	X	X
Initiate treatment		X			
Dispense/review/collect study diary		X	X	X	X
Review subject instructions		X	X	X	
Collect empty bottles			X	X	X
Evaluate IGA on face	X	X	X	X	X
Count inflammatory and non-inflammatory lesions on face	X	X	X	X	X
Count inflammatory and non-inflammatory lesions on the chest and/or back including shoulders (if applicable)[5]		X	X	X	X
Assess for any local cutaneous tolerance/application site reactions[6] on face, and if applicable, separately for the chest and/or back including shoulders[5]		X	X	X	X
CADI Questionnaire		X	X	X	X
Evaluate compliance			X	X	X
Adverse event assessment		X	X	X	X
End of study					X

[1] Visit 1 and 2 may have been combined if no washout period was required, but should not have been separated by more than 60 days.
[2] Visit window +/- 3 days
[3] Visit window +/- 5 days
[4] For all females regardless of reproductive potential
[5] For the selected site(s) that randomized subjects who were treating chest and/or back (including shoulders)
[6] Dryness, non-lesional erythema, peeling, stinging, burning, itching.

5. PLANNED ANALYSES

5.1. Final Analyses

Final analysis is planned for the study after the database lock. The final analysis will follow instructions presented in this SAP.

6. GENERAL CONSIDERATIONS FOR DATA ANALYSES AND HANDLING

6.1. General Summary Table and Individual Subject Data Listing Considerations

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

1. SAS program name.
2. Programmer.
3. Date of data extraction.
4. 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 group and a column will be included to summarize all treated subjects. The order of drug presentation will be investigational drug first followed by the vehicle control. A total column will appear as the last column. 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. 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, as a minimum, are sorted and presented by treatment group and subject id. Listings also include visit number, visit date, and days relative to the initiation of double-blind treatment.

6.2. General Post Text Summary Table and Individual Subject Data Listing Format Considerations

The default convention is to number tables and listings using a decimal system to reflect main levels of unique tables and listings and sub-levels of replicate tables and listings with two digits per level (e.g., Table XX.YY.ZZ. …).

1. The first level number should be consistent with the corresponding CSR appendix in which the tables or listings will appear. For example, the post text tables usually occupy Appendix 14 and the individual subject data listings are put in Appendix 16. All post text tables should have a main number level 14 and listings 16. The subject accounting and disposition table is usually first in the first section of the report and should be numbered Table 14.1. The supportive subject data listing would be Listing 16.1. A subset by sex table would have the number Table 14.1.2, etc.
2. Subject accounting and final disposition should appear as the second level number (Table 14.1 series). Baseline and demographic profile occupies the next sub-level (Table 14.2 series). Efficacy should come next (14.3 series) followed by safety (table 14.4 series). Reasons for subjects' being excluded from efficacy and protocol violation summary tables should appear as the last level (Table 14.5 series). Similar conventions should be applied to the subject data listings.
3. The title should be complete, accurate, and concise. The last line of the title should provide the analysis group being summarized (e.g., Intent-to-Treat Subjects or Per-Protocol Efficacy Subjects). If possible,

the units of measurement for data contained in the table can appear in parentheses to conserve space in the body of the table. For example, the summary of vital signs title could read "Summary of Sitting and Standing Blood Pressure (mmHg) and Heart Rate (bpm)." Whether in the title or body of a table or listing, units must always be specified for all appropriate data.

4. If possible, variables being summarized and statistics reported should appear in the left most column of a table. The next columns for treatment groups should report the data from left to right for the investigational drug, placebo, comparative agents, and (optional) all treated subjects, respectively.

In general, the listings should be sorted and presented by treatment assignment, investigational site, and subject number. Treatment assignment and site can appear in the banner of the listing. From left to right, the subject number, visit number, visit date, and relative day should appear. All tables and listings must have explanatory notes that give, as a minimum, data extraction date, output generation date, complete program name and path where it is stored, CRF pages from which the data were obtained, and supportive listings or tables supported, as appropriate. The definition of all derived variables and decodes for coded data must appear in the notes. Due to space limitations, tables and listings may require a page of notes as a one-time preface to the output.

6.3. Data Management

Biorasi will create SDTM data sets and ADaM analysis data sets using (SAS®) software. Data analyses and summary tables are generated using SAS version 9.4 or above.

6.4. Data Presentation Conventions

Continuous variables (e.g. age) are summarized using descriptive statistics (the number of subjects with available data, the mean, standard deviation (SD), median and minimum and maximum). Categorical variables (e.g. race) are summarized using counts and percentages. Percentages are calculated using the total subjects per treatment group.

The following conventions are applied to all data presentations and summaries.

For continuous variables, all mean and median values are formatted to one more decimal place than the measured value. Standard deviation values are formatted to two more decimal places than the measured value. Minimum and maximum values are presented with the same number of decimal places as the measured value.

For categorical variables, the number and percentage of responses are presented in the form XX (XX.X %) where the percentage is in the parentheses.

Date variables are formatted as DDMMMYYYY for presentation. Time is formatted in military time as HH:MM for presentation.

Wherever possible, data will be decimal aligned.

P-values, if applicable, will be presented to 4 decimal places. If the p-value is less than 0.0001 then it will be presented as <0.0001.

Unless otherwise stated, any statistical tests performed will use 2-sided tests at the 5% significance level.

The table and listing shells and table of contents as part of this SAP provide the expected layout and titles of the tables, listings and figures. Any changes to format, layout, titles, numbering, or any other minor deviation will not necessitate a revision to the SAP nor will it be considered a deviation from planned analyses. Only true differences in the analysis methods or data handling will necessitate such documentation. The appropriate listings supporting the tables will be included and are not specified in the individual sections throughout the document.

6.5. Analysis Populations

6.5.1. Screen Failures

A screen failure is a subject who received information about the study, including signing an informed consent and possibly performing some study-related procedures, but was not randomized and/or did not use study product.

These subjects will neither contribute to data presentations nor be included in the statistical analyses. The number of screen failures will be included in the data disposition table.

6.5.2. Safety Population

All subjects who receive at least one confirmed dose of study product and provide any post baseline safety information will be included in the safety population. No imputation will be made for missing safety data.

6.5.3. ITT Population

The ITT population consists of all subjects who were randomized and dispensed study medication.

6.5.4. Per-Protocol (PP) Population

The PP population will include all subjects in the ITT population who completed the Week 12 evaluation without any major protocol violations (i.e., any subject or investigator activity that could have possibly interfered with the therapeutic administration of the treatment or the precise evaluation of treatment efficacy).

Specifically, the PP population will include subjects in the ITT population who meet all of the following criteria:

1. Subject met all inclusion/exclusion criteria.
2. Subject did not take any prohibited concomitant medications during the evaluation period. The concomitant medication usage will be reviewed during the population determination review, remaining blinded to treatment designation, to determine prohibited medication usage that warrants exclusion from the PP population if they met the entrance criteria without any protocol violations. This review will take into consideration the timing, duration of treatment with the concomitant medication, and influence on the efficacy and safety assessments prior to deeming a prohibited concomitant medication as a protocol violation that warrants exclusion from PP.
3. Completed the Week 12 visit within the allowed window.
4. Subject was compliant with the dosing regimen. A subject will be considered compliant if the subject applied at least 80% but no more than 120% of the expected applications (168 applications expected) during the entire evaluation period.

Subjects who prematurely discontinued from the study due to documented lack of efficacy, worsening condition, or a treatment-related AE will be included in the PP population.

Other additional criteria may be added to the list to accommodate for unforeseen events that occurred during the conduct of the trial that result in noteworthy study protocol violations. These criteria will be documented with appropriate signature at the time subject populations are finalized, prior to database lock.

6.6. Baseline Definition

Baseline assessments are defined as the last non-missing result prior to administration of the first dose of study medication. If there are multiple assessments collected at the same scheduled time, the average of these

assessments will be used. If baseline is missing, then substitute the last screening value if available. If both baseline and screening is missing, then baseline is missing.

6.7. Derived and Transformed Data

6.7.1. Baseline Age

Subject's age in years will be calculated based on the date of the Baseline Visit date using the following formula:

Age (years) = FLOOR((INTCK('month', Date of Birth, Date of Baseline Visit) - (DAY(Date of Baseline Visit) < MIN(DAY(Date of Birth), DAY (INTNX ('month', Date of Baseline Visit, 1) - 1)))) /12)[7] where:

- FLOOR( ) is a SAS function that returns the largest integer that is less than or equal to the argument.
- INTCK() is a SAS function that returns the number of interval boundaries of a given kind that lie between two dates, times, or datetime values.
- DAY() is a SAS function that returns the day of the month from a SAS date value.
- INTNX() is a SAS function that increments a date, time, or datetime value by a given time interval, and returns a date, time, or datetime value.

6.7.2. Study Day

For this study:

- Day 1 is defined as the day of the first dose.
- For a visit date on or after the date of the first dose: Study Day = (date of interest – date of first dose) + 1
- For a visit date before the date of the first dose: Study Day = (date of interest – date of first dose)

6.7.3. Change from Baseline

Change from baseline is calculated as (post-baseline result – baseline result). Data will not be imputed for a specific post-baseline time point if the data was not recorded. Changes from baseline will be calculated based on the matched pairs of data points (subjects with data at both baseline and post-baseline).

Percent change from baseline is calculated as (change from baseline/baseline result * 100).

If either the baseline or the post-baseline result is missing, the change from baseline and/or percentage change from baseline will be set to missing.

6.7.4. Visit Windows

Visit windows for study DFD-03-CD-005 are displayed in Table 3.

Table 3: Visit Windows

Study Phase	Visit	Day	Visit Window
Screening	Visit 1[1]	Screening	Day -60 to 0
Baseline	Visit 2[1]	Baseline Day 1	Day 1
Treatment	Visit 3	Day 28 (Week 4)	Day 25 to 31
	Visit 4	Day 56 (Week 8)	Day 51 to 61
	Visit 5	Day 84 (Week 12)	Day 79 to 89

[1] Visit 1 and 2 may have been combined if no washout was required, but should not have been separated by more than 60 days.

6.7.5. Multiple Assessments

If there are multiple assessments collected at the same visit, the average of these assessments will be summarized in tables. The worst result for a visit will be used when a table is created to present abnormalities. Listings will list all data by visit, date and time.

6.8. Handling of Missing Data

6.8.1. Missing Efficacy Endpoints

Missing efficacy endpoints will be imputed for week 12 IGA and lesion count analyses only. Details can be found in Section 8.3.

6.8.2. Missing Start and Stop Dates for Prior and Concomitant Medication

Start date:

1. If start date is completely missing, start date will not be imputed.
2. If (year is present and month and day are missing) or (year and day are present and month is missing), set month and day to January 1.
3. If year and month are present and day is missing, set day to the 1st day of month.

Stop date:

1. If end date is completely missing, end date will not be imputed.
2. If (year is present and month and day are missing) or (year and day are present and month is missing), set month and day to December 31st.
3. If year and month are present and day is missing, set day to the last day of month.

Further details on classifying medications as either prior or concomitant are outlined in the protocol Section 6.6.

6.8.3. Missing Start and Stop Dates for Adverse Events

Start date:

1. If start date is completely missing, start date is set to date of first dose.
2. If (year is present and month and day are missing) or (year and day are present and month is missing):
    a. If year = year of first dose, then set month and day to month and day of first dose.
    b. If year < year of first dose, then set month and day to December 31st.
    c. If year > year of first dose, then set month and day to January 1st.
3. If month and year are present and day is missing:
    a. If year = year of first dose and
        i. If month = month of first dose, then set day to day of first dose date.
        ii. If month < month of first dose, then set day to last day of month.
        iii. If month > month of first dose, then set day to 1st day of month.

b. If year < year of first dose, then set day to last day of month.
c. If year > year of first dose, then set day to 1st day of month.

Stop date:

If the outcome of the AE was ongoing or unknown, then the rules outlined below will not be applied.

1. If stop date is completely missing, stop date is set to date of study discontinuation.
2. If (year is present and month and day are missing) or (year and day are present and month is missing):
    a. If year = year of study discontinuation, then set month and day to month and day of study discontinuation.
    b. If year < year of study discontinuation, then set month and day to December 31st.
    c. If year > year of study discontinuation, then set month and day to December 31st.
3. If month and year are present and day is missing:
    a. If year = year of study discontinuation and
        i. If month = month of study discontinuation, then set day to day of study discontinuation date.
        ii. If month < month of study discontinuation, then set day to last day of month.
        iii. If month > month of study discontinuation, then set day to last day of month.
    b. If year < year of study discontinuation, then set day to last day of month.
    c. If year > year of study discontinuation, then set day to last day of month.

7. STUDY POPULATION

7.1. Subjects Disposition

The subject disposition summary will include the number screened, the number of screen failures, the number enrolled, the number in each patient population for analysis, the number who completed the study, the number who discontinued the study and reason for discontinuation from the study. Disposition data will be summarized by treatment and overall.

A by-subject data listing of study completion information including the reason for study discontinuation will be presented. A by-subject listing of inclusion/exclusion criteria not met will also be presented.

7.2. Protocol Deviations

A summary of all protocol deviations by type will be generated. Protocol deviation data will be summarized by treatment and overall. A by-subject data listing of protocol deviations will also be presented.

7.3. Demographic and Baseline Characteristics

The following demographic and baseline characteristics will be summarized by treatment and overall:

- Age (Years)
- Age Group (12 – 16 Years, 17 - 64 Years, 65 Years or Older)
- Gender (Male, Female)
- Race (White, Black or African American, Asian, American Indian or Alaskan Native, Native Hawaiian or Other Pacific Islander and Other)
- Ethnicity (Hispanic or Latino, Non-Hispanic or Non-Latino)
- Fitzpatrick Classification Scale (I, II, III, IV, V, VI)
- Investigator's Global Assessment (IGA) at Baseline (0 = Clear, 1 = Almost Clear, 2 = Mild, 3= Moderate, 4 = Severe)
- Inflammatory Lesion Count
- Non-inflammatory Lesion Count

Age will be computed using date of birth and baseline visit date with details in Section 6.7.1.

The Fitzpatrick skin scale classifies a person's complexion and tolerance of sunlight. It is commonly used by many practitioners to determine how someone will respond or react to facial treatments. The Fitzpatrick skin scale is presented in Table 4 below.

Table 4: Fitzpatrick Classification Scale

Skin Type	Skin Color	Characteristics
I	White; very fair; red or blond hair; blue eyes; freckles	Always burns, never tans
II	White; fair; red or blond hair; blue, hazel, or green eyes	Usually burns, tans with difficulty

Skin Type	Skin Color	Characteristics
III	Cream white; fair with any eye or hair color; very common	Sometimes mild burn, gradually tans
IV	Brown; typical Mediterranean Caucasian skin	Rarely burns, tans with ease
V	Dark Brown; mid-eastern skin types	Very rarely burns, tans very easily
VI	Black	Never burns, tans very easily

7.4. Medical History

Medical history verbatim text will be coded and classified by system organ class (SOC) and preferred term (PT) using the MedDRA (Version 20.0).

Medical history summary tables will use the following algorithms for counting subject histories within the summary tables:

- Any medical history row: Each subject with a medical history is counted only once although he/she may have several medical histories.
- System organ class rows: Each subject is counted only once at each SOC level although he/she may have several different PT events within the same SOC.
- Preferred term rows: Each subject is counted once within each unique PT.

Medical history data will be summarized by treatment and overall. A by-subject data listing of medical history will also be presented.

8. EFFICACY ANALYSES

8.1. Efficacy Assessments

The investigator was responsible for all clinical evaluations, with best attempts made to assign the same evaluator for a subject throughout the study to obtain consistency in grading scores and measurements.

Efficacy assessments were conducted using IGA for overall disease severity and inflammatory and non-inflammatory lesion counts on the face. The IGA was always done prior to lesion counts.

8.1.1. Investigator's Global Assessment (IGA) of the Face

The IGA scale used in the study is a measure of static evaluation of qualitative overall acne severity. IGA is an ordinal scale with five severity grades (reported only in integers, e.g., 0 to 4). Each grade is defined by a distinct and clinically relevant morphologic description to minimize inter-observer variability (Table 5). The grades on the scale have been sufficiently defined to appropriately and unambiguously represent each severity grade on the scale. The investigator was required to perform IGA scoring at each visit. The IGA was always done prior to lesion counts.

Table 5: IGA Scale for Facial Acne Vulgaris

Grade	Description[1]
0	Clear skin with no inflammatory or non-inflammatory lesions
1	Almost clear; rare non-inflammatory lesions with no more than rare papules
2	Mild severity; some non-inflammatory lesions with no more than a few inflammatory lesions (papules/pustules only, no nodular lesions)
3	Moderate severity; up to many non-inflammatory lesions and may have some inflammatory lesions, but no more than one small nodular lesion
4	Severe; up to many non-inflammatory and inflammatory lesions, but no more than a few nodular lesions

[1] Areas other than the face and nose were not included in assessment.

Enrollment of subjects with mild acne (IGA Grade 2) at each site was restricted to no more than 20% of total enrollment at that site; management of this requirement was handled by the IWRS.

8.1.2. Lesion Counts of the Face

Non-inflammatory lesions (closed comedones and open comedones), inflammatory lesions (papules and pustules), and nodulocystic lesions (nodules and cysts) on the face (above the mandibular line), including the nose, were counted and recorded separately at each visit from Screening/Baseline through Week 12. Non-inflammatory lesions of acne are the open (blackheads) or closed (whiteheads) comedones. Closed comedones may be more difficult to detect visually and may require stretching of the skin to aid in visualization. Inflammatory lesions are divided into papules, pustules, and nodules/nodulocystic lesions, depending on the severity and location of the inflammation within the dermis. Nodulocystic lesions will be counted separately from inflammatory lesions of papules and pustules. The papules and pustules have surrounding halos of erythema allowing for their characterization as inflammatory.

Nodules are typically erythematous and often tender and/or painful. Additionally, they are deep- seated in the skin (i.e., centered in the dermis or subcutis). Nodules have been defined as being greater than 5 mm in diameter. The borders of these lesions may be difficult to determine because of the associated

erythema/inflammation. The investigator/evaluator should have used standard, good lighting to visualize lesions and a systematic counting procedure to ensure consistent and accurate counts.

8.1.3. Lesion Counts of the Chest and/or Back (including shoulders)

At selected site(s), for subjects who had acne lesions on their chest and/or back (including shoulders), lesion counts were assessed separately for these areas.

Non-inflammatory lesions (closed comedones and open comedones), inflammatory lesions (papules and pustules), and nodulocystic lesions (nodules and cysts) on the chest and/or back including shoulders (if applicable) were counted and recorded separately at each visit from Baseline through Week 12. Nodulocystic lesions were counted separately from inflammatory lesions of papules and pustules. The back area is from most prominent cervical spinous process superiorly to the superior aspect of iliac crest inferiorly and the shoulder area was also included. The chest area is from the manubrium of the sternum superiorly to the xiphiod process inferiorly. The lesion types were as described above. The investigator/evaluator was to use standard, good lighting to visualize lesions and a systematic counting procedure to ensure consistent and accurate counts.

8.1.4. Cardiff Acne Disability Index (CADI)

The CADI is a short 5 item questionnaire that will be conducted by all subjects at Baseline, Week 4, 8, and 12. The questionnaire rapidly assesses the disability caused by the acne. It consists of 5 questions. The scoring for each question is done from 0 to 3 (a=3, b=2, c=1, d=0). The CADI score is calculated by summing the score of each question resulting in a possible maximum of 15 and a minimum of 0. The higher the score, the more the quality of life is impaired.

The CADI questionnaire is provided in Appendix 2 of the protocol.

8.2. Subgroup Analyses

For the safety and efficacy endpoints the following subgroup analyses will be done:

Table 6: Summary of Subgroup Analyses

Subgroup	Specification Values
Age Group 1	12 – 16 Years, 17 – 64 Years, ≥ 65 Years
Age Group 2	< Median Age, ≥ Median Age
Gender	Male, Female
Race	White, Black or African American, Asian, Other
Ethnicity	Hispanic or Latino, Not Hispanic or Latino
Fitzpatrick Classification Scales	I-IV, V-VI

For the safety analyses, safety will be summarized for all subgroups except Fitzpatrick Classification Scales.

For the efficacy analyses, efficacy will be summarized for all subgroups.

8.3. Analysis of the Efficacy Endpoints

The following efficacy endpoints will be summarized using descriptive statistics for both the ITT and PP populations:

- Proportion of Subjects with IGA Success at Weeks 4, 8 and 12. IGA success is defined as an IGA score of 0 (Clear) or 1 (Almost Clear) with at least a 2-grade reduction from baseline.
- Absolute Change from Baseline in Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Absolute Change from Baseline in Non-Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Percent Change from Baseline in Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Percent Change from Baseline in Non-Inflammatory Lesion Counts at Weeks 4, 8 and 12. The following location of lesions will be summarized separately: face and chest/back/shoulders.
- Change from Baseline to Weeks 4, 8 and 12 in CADI.

For all efficacy endpoints for the ITT and PP populations, data will be summarized at week 4, 8 and 12 with data as is where missing data is not imputed.

Also for missing IGA and lesion counts in the ITT population, data will be summarized at week 12 where the primary handling method for missing data, except for baseline, will be the multiple imputation (MI) approach via regression. In details, the MI regression model will include the following predictors in the model: treatment, age, gender, baseline inflammatory lesion counts, baseline non-inflammatory lesion counts, and the results of the same variable from previous visits. The average score of the MI copies will be used to calculate the summary statistics.

Finally for missing IGA, lesion counts and CADI in the PP population, data will be summarized at week 12 where the primary handling method for missing data will be the Last Observation Carried Forward (LOCF). For the PP population, number of subjects who were discontinued prematurely due to documented lack of efficacy, worsening condition, or a TEAE is expected to be small. For these subjects the efficacy data from their termination visit will be assigned to the nearest corresponding scheduled visit that has been missed, and carried forward to the subsequent visits for the analysis.

9. SAFETY ANALYSES

All safety analyses will be based on the safety population.

9.1. Study Drug Exposure and Compliance

9.1.1. Number of Applications Applied

The Number of Applications Applied will be summarized by treatment using the following statistics: n, mean, standard deviation [SD], median, minimum and maximum.

9.1.2. Days of Exposure

Days of Exposure = (stop date of study drug – start date of study drug) + 1.

Days of Exposure will be summarized by treatment using the following statistics: n, mean, standard deviation [SD], median, minimum and maximum.

Also Days of Exposure will be summarized by treatment using the following categories:

- < 28 Days
- 28 to 56 Days
- 57 to 84 Days
- > 84 Days

9.1.3. Compliance

Compliance will be calculated for all subjects in the safety population.

Compliance (%) = A/P x 100, where:

- A = Total number of applications actually applied.
- P = Total number of applications for the respective evaluation period.

Compliance will be summarized by treatment using the following statistics: n, mean, standard deviation [SD], median, minimum and maximum.

In addition, the number and percentage of subjects that have a compliance rate between 80% and 120% will be summarized by a Yes/No category. Note a subject is considered compliant with the dosing regimen if the subject has applied at least 80% but no more than 120% of the expected applications for the respective evaluation period.

9.2. Local Cutaneous Safety Evaluation

Non-lesional erythema, peeling, dryness, stinging, burning and itching scores will be summarized by treatment group and visit including sample size, frequency count and percentage for each visit. A similar summary will be provided excluding subjects with signs or symptoms present at Baseline.

Non-lesional erythema, peeling, dryness, stinging, burning and itching scores and their corresponding descriptions are listed in Table 7, Table 8, Table 9, Table 10, Table 11 and Table 12 respectively.

Table 7: Scoring of Non-Lesional Erythema

Severity	Score	Description
None	0	No erythema
Mild	1	Light pinkness present
Moderate	2	Definite redness, easily recognized
Severe	3	Intense redness

Table 8: Scoring of Peeling

Severity	Score	Description
None	0	No peeling
Mild	1	Barely perceptible shedding, noticeable only on light scratching or rubbing
Moderate	2	Obvious but not profuse shedding
Severe	3	Heavy scale production

Table 9: Scoring of Dryness

Severity	Score	Description
None	0	No dryness
Mild	1	Slight barely perceptible fine superficial scale
Moderate	2	Clearly perceptible fine scale giving skin a powdery appearance
Severe	3	Marked roughness, cracked skin with fissures

Table 10: Scoring of Stinging

Severity	Score	Description
None	0	No stinging
Mild	1	Slight sharp, tingling/stinging sensation; not really bothersome
Moderate	2	Definite sharp, tingling/stinging sensation; that is somewhat bothersome
Severe	3	Sharp, tingling/stinging sensation that has caused definite discomfort

Table 11: Scoring of Burning

Severity	Score	Description
None	0	No burning
Mild	1	Slight warm, burning sensation; not really bothersome
Moderate	2	Definite warm, burning sensation; that is somewhat bothersome
Severe	3	Hot, burning sensation that has caused definite discomfort

Table 12: Scoring of Itching

Severity	Score	Description
None	0	No itching
Mild	1	Slight itching; not really bothersome
Moderate	2	Definite itching that is somewhat bothersome, without loss of sleep
Severe	3	Intense itching that has caused pronounced discomfort; night rest interrupted and excoriation of the skin from scratching may be present

Overall cutaneous tolerance was graded at the Week 12 visit, or the last visit if earlier, using grades shown in Table 13 below.

Table 13: Overall Tolerance

Grade	Score	Description
Excellent	0	No signs of irritation during the study
Good	1	Slight signs of irritation during the study, which resolved by the end of the study
Fair	2	Signs of irritation throughout the study
Poor	3	Subject discontinued due to irritation

Irritation was defined as any sign or symptom of intolerance.

Grades for Overall Tolerance will be summarized by treatment and overall.

9.3. Adverse Event (AE)

9.3.1. Adverse Event Definitions

The following definitions will apply to the reporting of adverse events.

9.3.1.1. Adverse Event (AE)

An adverse event (AE) is any untoward medical occurrence in a subject participating in a clinical trial. The event does not necessarily have to have a causal relationship with the study product. An AE can therefore be any sign, symptom, or disease, or any worsening of an existing sign, symptom, or disease, whether or not considered related to the study product or trial procedures, including injuries.

Any medical condition that is present at the time of Screening or Baseline should be considered as medical history and reported on the medical history eCRF and should not be reported as an AE except for AEs observed at the Baseline Visit due to study procedures performed at the Screening visit, which should be reported. Anticipated day-to-day fluctuations of pre-existing conditions should not be reported as AEs. Unexpected worsening of pre-existing conditions should be reported as AEs. The disease or condition being studied or expected progression, signs, or symptoms of the disease or condition being studied such as worsening of acne should not be reported as an AE unless it is more severe than expected, results in discontinuation from the study or requires alternative therapy.

9.3.1.2. Treatment-Emergent Adverse Event (TEAE)

A treatment-emergent adverse event (TEAE) is defined as any AE which started on or after the first administration of study drug and include those events started prior to the first administration of study drug but which worsened after the first administration of study drug.

9.3.1.3. Serious Adverse Event (SAE)

A serious adverse event (SAE) is any AE occurring at any dose that results in any of the following outcomes:

1. Death
2. Life-threatening (subject at immediate risk of death)
3. Inpatient hospitalization or prolongation of hospitalization
4. Results in persistent or significant disability/incapacity
5. Results in congenital anomaly/birth defect

Important medical events that may not result in death, are not life-threatening, or do not require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above. Examples of such medical events include allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias or convulsions that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.

9.3.2. Assessment of Adverse Events

9.3.2.1. Severity of an Adverse Event

The severity of an adverse event was classified into one of three categories:

1. Mild (Grade 1): Awareness of sign or symptom, but easily tolerated. Not likely to interfere with normal activity or require medical attention.
2. Moderate (Grade 2): Discomfort enough to cause interference with usual activity. May require medical intervention.
3. Severe (Grade 3): Incapacitating such that normal activity is prevented. Likely requires medical intervention and/or close follow-up.

9.3.2.2. Relationship to Study Product (Causality)

The degree of "relatedness" of the AE to the study product was described using the following categories:

1. Not Related: The event is clearly due to extraneous causes (e.g., diseases, environment, etc.). Specify if known. Or, the event is most probably produced by other factors such as the subject's clinical state, therapeutic interventions, or concomitant therapy and does not follow a known response pattern to the study product.
2. Possibly Related: The event is temporally related to study product use but can be explained by another etiology. Information on the effect of study product withdrawal may be lacking.
3. Probably Related: The event is temporally related to study product use and is consistent with known effects of the study product and/or improves upon withdrawal of the study product.

4. Definitely Related: The event follows a reasonable temporal sequence from the time of study product administration and/or follows a known response pattern to the study product, and could not have been produced by other factors such as the subject's clinical state, therapeutic intervention, or concomitant therapy, and either occurs immediately following study product administration or improves on stopping the product, or there is a positive reaction at the application site.

9.3.3. Missing and Partial AE Start and Stop Dates

Imputation rules for missing or partial AE start and end dates are outlined in Section 6.8.3.

9.3.4. Summaries of Adverse Events

Adverse event verbatim text will be coded and classified by system organ class (SOC) and preferred term (PT) using the MedDRA (Version 20.0). AE summary tables will use the following algorithms for counting subject events within the summary tables:

- Any event row: Each subject with an event is counted only once at the maximum grade although they may have several events. For drug related AE tables, each subject with an event is counted only once at the most related although they may have several events.
- System organ class rows: Each subject is counted only once at the maximum grade at each system organ class level although they may have several different preferred term events within the same SOC.
- Preferred term rows: Each subject is counted once within each unique preferred term at the maximum grade. Subjects experiencing the same AE preferred term several times with different grades would only be counted once with the maximum grade.

For partially missing start or stop dates, the imputation rule specified in Section 6.8.3 will be applied before assessing if an AE was a TEAE.

TEAE data will be summarized by treatment and overall.

9.3.4.1. Overview and Summaries of Adverse TEAEs

An overall summary table (overview) of all TEAEs will be presented, summarizing:

- Total Number of TEAEs
- Total Number of TESAEs
- Total Number of TEAESIs
- Number of Subjects with at Least One TEAE
- Number of Subjects with at Least One Related TEAE
- Number of Subjects with at Least One Severe (Grade 3) TEAE
- Number Subjects with at Least One TEAE Leading to Treatment Discontinuation
- Number Subjects with at Least One TEAE Leading to Death
- Number of Subjects with at Least One TESAE
- Number of Subjects with at Least One Related TESAE
- Number of Subjects with at Least One TEAESI

TEAEs will be summarized by SOC and PT. For SOC, each subject is counted only once at each SOC level although they may have several different PT events within the same SOC. Likewise for any PT event, each subject with an event is counted only once although they may have several PT events that are the same.

Summaries for the common TEAEs will be created for TEAEs with an incidence [> 1%] in at least one treatment group. Common TEAEs will be summarized by SOC and PT.

Summaries for TEAEs by maximum severity will be created for all TEAEs. Severity will be summarized by SOC and PT. If a subject has multiple occurrences of the same SOC or PT, then only the most severe event will be summarized in the tables for that SOC or PT. TEAEs with missing severity treatment will be counted as severe.

Summaries for TEAEs by the closest relationship to study drug will be created for all TEAEs. Relationship to study drug will be summarized by SOC and PT. TEAEs will be classified as "Related" to study drug if relationship is categorized as Definitely Related, Probably Related or Possibly Related. Otherwise TEAEs will be classified as "Not Related". If a subject has multiple occurrences of the same SOC or PT, then only the most related event will be summarized in the tables for that SOC or PT. TEAEs with missing relationship to study drug will be counted as "Related".

TEAE outcomes will be summarized by SOC and PT. TEAE outcome categories are:

- Recovered/Resolved
- Recovered/Resolved with Sequelae
- Not Recovered/Not Resolved
- Fatal
- Unknown

If a subject has multiple occurrences of the same SOC or PT, then only the most negative outcome will be summarized in the tables for that SOC or PT. TEAEs with missing outcome will be counted as unknown. Most negative outcome in terms of decreasing rank are: Fatal, Not Recovered/Not Resolved, Recovered/Resolved with Sequelae, Recovered/Resolved, Unknown.

TEAE actions taken with study drug will be summarized by SOC and PT. TEAE action taken with study drug categories are:

- Dose Not Changed
- Drug Withdrawn
- Dose Interrupted
- Dose Reduced
- Dose Increased
- Unknown

If a subject has multiple occurrences of the same SOC or PT, then only the most negative action taken with study drug will be summarized in the tables for that SOC or PT. TEAEs with missing action taken with study drug will be counted as unknown. Most negative action taken with study drug in terms of decreasing rank are: Drug Withdrawn, Dose Interrupted, Dose Reduced, Dose Increased, Dose Not Changed, and Unknown.

TEAE actions taken with subject will be summarized by SOC and PT. TEAE action taken with subject categories are:

- None
- Hospitalization
- Change in Concomitant Medication
- Other
- Unknown

If a subject has multiple occurrences of the same SOC or PT, then only the most negative action taken with subject will be summarized in the tables for that SOC or PT. TEAEs with missing action taken with subject will be counted as unknown. Most negative action taken with study drug in terms of decreasing rank are: Hospitalization, Change in Concomitant Medication, Other, None, Unknown.

Severe TEAEs collected during the course of the study will be summarized by SOC and PT.

Treatment Emergent Serious Adverse Events (TESAEs) collected during the course of the study will be summarized by SOC and PT.

TEAEs leading to study discontinuation will be summarized by SOC and PT.

Treatment Emergent Adverse Events of Special Interest (TEAESIs) will be summarized by SOC and PT.

9.4. Prior and Concomitant Medications

Prior medications are defined as medications with stop dates occurring before the date of first administration of the study drug. Concomitant medications are defined as medications with start dates occurring before, on, or after the date of first administration of study drug and stopping after the first administration of study drug or continuing beyond that.

For the purpose of summarizing prior and concomitant medications, incomplete medication start and stop dates will be imputed as detailed in Section 6.8.2. Based on imputed start and stop dates, specifies the rules on how a medication is classified as either a prior or concomitant medication and how it will be assigned to a specific study drug.

Table 14: Rules for Prior and Concomitant Medications

Prior vs. Concomitant	Rules
Prior	Stop date was before the first administration of study drug.
Concomitant	1. Stop date was on or after the first administration of study drug. 2. Or stop date was missing. 3. Or both start and stop dates were missing.

All medications are coded using the World Health Organization Drug Dictionary (WHO-DD) version March 2017 – C format. WHO-DD ATC Class Level 1, WHO-DD ATC Class Level 2 and preferred term (PT) will be used to summarize the data by treatment.

9.5. Clinical Laboratory Data

No blood samples were collected for hematology and serum biochemistry tests.

Urine samples were collected for urine pregnancy tests. Urine pregnancy tests were done at all study visits. No tables reporting urine pregnancy test results will be produced. However, a data listing reporting urine pregnancy test results will be produced.

9.6. Vital Signs

The following vital sign parameters will be summarized by visit and treatment group:

- Diastolic Blood Pressure (mm Hg)
- Systolic Blood Pressure (mm Hg)
- Pulse Rate (beats/min)

In general, if multiple results are reported within the given analysis visit window for the same parameter, the mean of the results will be used for summary statistics except for baseline, for which the last assessment will be used.

For all vital sign parameter, the continuous results will be summarized using descriptive statistics by visit and treatment group. The summary statistics are n, mean, median, SD, minimum and maximum. Boxplots for vital signs versus time by treatment for all time points will also be generated. Boxplots will display Baseline, Day 28, Day 56 and Day 84 assessments.

Changes from baseline will also be summarized by visit and treatment. The summary statistics are n, mean, median, SD, minimum and maximum. With respect to the mean change from baseline, the 95% confidence interval will also be computed. Boxplots for change from baseline versus time by treatment for all time points will also be generated. Boxplots will display Day 28, Day 56 and Day 84 assessments.

Potentially Clinically Significant (PCS) vital signs will be summarized by parameter. The summary will indicate the number of subjects with PCS-low or PCS-high values by visit and treatment group. The criteria for identifying PCS abnormalities for vital signs are summarized in Table 15.[8, 9]

Table 15: Criteria for Potentially Clinical Significant Vital Sign Abnormalities

Parameter	Age	Criteria	
		PCS Low	**PCS High**
Pulse (beats/min)	5 to 14 years	≤ 50 bpm at any time post dose.	≥ 140 bpm at any time post dose.
	15 to 18 years	≤ 50 bpm at any time post dose.	≥ 120 bpm at any time post dose.
	18 and above	≤ 50 bpm at any time post dose.	≥ 110 bpm at any time post dose.
	Any	Any ≥ 15 bpm decrease from baseline at any time post dose.	Any ≥ 15 bpm increase from baseline at any time post dose.
Systolic Blood Pressure (mm Hg)	7 to 12 years	≤ 117 mm HG at any time post dose.	≥ 130 mm Hg at any time post dose.
	13 to 17 years	≤ 120 mm HG at any time post dose.	≥ 144 mm Hg at any time post dose.
	18 and above	≤ 90 mm HG at any time post dose.	≥ 150 mm Hg at any time post dose.
	Any	Any ≥ 20 mm Hg decrease from baseline at any time post dose.	Any ≥ 20 mm Hg increase from baseline at any time post dose.
Diastolic Blood Pressure (mm Hg)	7 to 12 years	≤ 75 mm HG at any time post dose.	≥ 86 mm Hg at any time post dose.
	13 to 17 years	≤ 80 mm HG at any time post dose.	≥ 92 mm Hg at any time post dose.

Parameter	Age	Criteria	
		PCS Low	**PCS High**
	18 and above	≤ 50 mm HG at any time post dose.	≥ 100 mm Hg at any time post dose.
	Any	Any ≥ 15 mm Hg decrease from baseline at any time post dose.	Any ≥ 15 mm Hg increase from baseline at any time post dose.

9.7. Physical Examination

Physical examination results will be presented for each body system examined at baseline and termination visit. The number and percent of subjects judged to be normal, abnormal not clinically significant, abnormal clinically significant, or not performed will be summarized. It should be kept in mind that even though the subject may have a history of a particular condition, the clinician must actually observe symptoms upon examination in order to have the particular system judged abnormal.

Physical examination data will be summarized by treatment and overall.

The supportive data listing will include body system, result of the observation (e.g., normal, abnormal not clinically significant, abnormal clinically significant) or not performed, and any investigator comment.

10. REFERENCES

1. Protocol Number DFD-03-CD-008, Version 1.0 "A Randomized, Double-Blind, Active-Controlled Study to Assess the Safety and Local Tolerability of DFD-03 (tazarotene) Lotion, 0.1% compared to Tazorac® (tazarotene) Cream, 0.1% in the Topical Treatment of Acne Vulgaris for 12 Weeks" 02 June 2017.
2. Protocol Number DFD-03-CD-008, Version 2.0, Amendment 01 "A Randomized, Double-Blind, Active-Controlled Study to Assess the Safety and Local Tolerability of DFD-03 (tazarotene) Lotion, 0.1% compared to Tazorac® (tazarotene) Cream, 0.1% in the Topical Treatment of Acne Vulgaris for 12 Weeks" 06 November 2017.
3. Data Management Plan, Draft Version 1.0, Protocol No. DFD-03-CD-008, "A Randomized, Double-Blind, Active-Controlled Study to Assess the Safety and Local Tolerability of DFD-03 (tazarotene) Lotion, 0.1% compared to Tazorac® (tazarotene) Cream, 0.1% in the Topical Treatment of Acne Vulgaris for 12 Weeks" 05 October 2017.
4. CRF DRL DFD-03-CD-008, Version Date 22 September 2017.
5. CRF DRL DFD-03-CD-008, Version Date 28 September 2017.
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8. Oracle. (2016, February 22). Oracle Health Sciences Empirica Study - Data sheet | Oracle [PDF]. Redwood City, CA: Oracle. http://www.oracle.com/us/industries/life-sciences/empirica-study-on-demand-ds-396095.pdf.
9. Oracle. (2016, March 22). Clinical Significance Criteria. Retrieved January 26, 2018, from https://docs.oracle.com/health-sciences/empirica-study-80/WEWUG/Clinical_Significance_Criteria.htm.

11. APPENDIX

11.1. Table of Contents for Data Display Specifications

Refer to the MS Excel spreadsheet.

11.2. DATA DISPLAY SPECIFICATIONS INDEX

Table 20: List of Tables, Listings and Figures

Display Number	Title	Populations	Subgroup	Unique/ Repeat
Study				
Table 14.1.1.1	Subject Enrollment and Disposition	All Subjects	N/A	Unique
Table 14.1.1.2	Subject Enrollment by Study Site	Enrolled Subjects	N/A	Unique
Table 14.1.2	Summary of Protocol Deviations (PD)/Violations (PV)	ITT	N/A	Unique
Table 14.1.3.1	Summary of Demographic and Baseline Characteristics	ITT	N/A	Unique
Table 14.1.3.2	Summary of Demographic and Baseline Characteristics	PP	N/A	Repeat
Table 14.1.3.3	Summary of Demographic and Baseline Characteristics	Safety	N/A	Repeat
Table 14.1.4	Summary of Study Drug Exposure and Compliance by Location	Safety	N/A	Unique
Table 14.1.5	Summary of Prior Medications	Safety	N/A	Unique
Table 14.1.6	Summary of Concomitant Medications	Safety	N/A	Repeat

Display Number	Title	Populations	Subgroup	Unique/ Repeat
Efficacy Tables				
Table 14.2.1.1.1	Primary Analysis of Efficacy Endpoint - Descriptive Statistics of the IGA Success Rate at Week 4, ITT Population	ITT	N/A	Unique
Table 14.2.1.1.2	Primary Analysis of Efficacy Endpoint - Descriptive Statistics of the IGA Success Rate at Week 8, ITT Population	ITT	N/A	Repeat
Table 14.2.1.1.3.1	Primary Analysis of Efficacy Endpoint - Descriptive Statistics of the IGA Success Rate at Week 12, with MI, ITT Population	ITT	N/A	Repeat
Table 14.2.1.1.3.2	Primary Analysis of Efficacy Endpoint - Descriptive Statistics of the IGA Success Rate at Week 12, ITT Population	ITT	N/A	Repeat
Table 14.2.1.1.4	Primary Analysis of Efficacy Endpoint - Descriptive Statistics of the IGA Success Rate at Week 4, PP Population	PP	N/A	Repeat
Table 14.2.1.1.5	Primary Analysis of Efficacy Endpoint - Descriptive Statistics of the IGA Success Rate at Week 8, PP Population	PP	N/A	Repeat
Table 14.2.1.1.6	Primary Analysis of Efficacy Endpoint - Descriptive Statistics of the IGA Success Rate at Week 12, PP Population	PP	N/A	Repeat
Table 14.2.1.2.1	Absolute change from baseline in inflammatory and non-inflammatory lesion counts at the Week 4 visit. ITT Population.	ITT	N/A	Unique
Table 14.2.1.2.2	Absolute change from baseline in inflammatory and non-inflammatory lesion counts at the Week 8 visit. ITT Population.	ITT	N/A	Repeat
Table 14.2.1.2.3	Absolute change from baseline in inflammatory and non-inflammatory lesion counts at the Week 12 visit. ITT Population.	ITT	N/A	Repeat

Table 14.2.1.2.3.1	Absolute change from baseline in inflammatory and non-inflammatory lesion counts at the Week 12 visit. With MI-ITT Population.	ITT	N/A	Repeat
Table 14.2.1.2.4	Absolute change from baseline in inflammatory and non-inflammatory lesion counts at the Week 4 visit. PP Population.	PP	N/A	Repeat
Table 14.2.1.2.5	Absolute change from baseline in inflammatory and non-inflammatory lesion counts at the Week 8 visit. PP Population.	PP	N/A	Repeat
Table 14.2.1.2.6	Absolute change from baseline in inflammatory and non-inflammatory lesion counts at the Week 12 visit. PP Population.	PP	N/A	Repeat
Table 14.2.1.3.1	Percent change from Baseline to Week 4 in inflammatory and non-inflammatory lesion counts, ITT Population.	ITT	N/A	Unique
Table 14.2.1.3.2	Percent change from Baseline to Week 8 in inflammatory and non-inflammatory lesion counts, ITT Population.	ITT	N/A	Repeat
Table 14.2.1.3.3	Percent change from Baseline to Week 12 in inflammatory and non-inflammatory lesion counts, ITT Population.	ITT	N/A	Repeat
Table 14.2.1.3.4	Percent change from Baseline to Week 4 in inflammatory and non-inflammatory lesion counts in the PP Population.	PP	N/A	Repeat
Table 14.2.1.3.5	Percent change from Baseline to Week 8 in inflammatory and non-inflammatory lesion counts in the PP Population.	PP	N/A	Repeat
Table 14.2.1.3.6	Percent change from Baseline to Week 12 in inflammatory and non-inflammatory lesion counts in the PP Population.	PP	N/A	Repeat
Table 14.2.1.4.1	Change from Baseline to Week 4 in Cardiff Acne Disability Index (CADI), ITT Population	ITT	N/A	Unique
Table 14.2.1.4.2	Change from Baseline to Week 8 in Cardiff Acne Disability Index (CADI), ITT Population	ITT	N/A	Repeat

Table 14.2.1.4.3	Change from Baseline to Week 12 in Cardiff Acne Disability Index (CADI), ITT Population	ITT	N/A	Repeat
Table 14.2.1.4.4	Change from Baseline to Week 4 in Cardiff Acne Disability Index (CADI), PP Population	PP	N/A	Repeat
Table 14.2.1.4.5	Change from Baseline to Week 8 in Cardiff Acne Disability Index (CADI), PP Population	PP	N/A	Repeat
Table 14.2.1.4.6	Change from Baseline to Week 12 in Cardiff Acne Disability Index (CADI), PP Population	PP	N/A	Repeat

Display Number	Title	Populations	Subgroup	Unique/ Repeat
Safety Tables				
Table 14.2.2.1	Subject Compliance - Total Number of Applications, Number and Percentage of Subjects who are Compliant for the Baseline to Week 12 evaluation period	Safety	N/A	Unique
Table 14.2.2.2.1	Local Cutaneous Safety Evaluation by Treatment Group and Visit-Non- lesional erythema	Safety	N/A	Unique
Table 14.2.2.2.2	Local Cutaneous Safety Evaluation by Treatment Group and Visit-Peeling	Safety	N/A	Repeat
Table 14.2.2.2.3	Local Cutaneous Safety Evaluation by Treatment Group and Visit-Dryness	Safety	N/A	Repeat
Table 14.2.2.2.4	Local Cutaneous Safety Evaluation by Treatment Group and Visit-Burning	Safety	N/A	Repeat
Table 14.2.2.2.5	Local Cutaneous Safety Evaluation by Treatment Group and Visit-Stinging	Safety	N/A	Repeat
Table 14.2.2.2.6	Local Cutaneous Safety Evaluation by Treatment Group and Visit-Itching	Safety	N/A	Repeat
Table 14.2.2.3.1	Local Cutaneous Safety Evaluation by Treatment Group and Visit- Excluding Subjects with Signs or Symptoms at Baseline-Non-lesional erythema	Safety	N/A	Repeat
Table 14.2.2.3.2	Local Cutaneous Safety Evaluation by Treatment Group and Visit- Excluding Subjects with Signs or Symptoms at Baseline-Peeling	Safety	N/A	Repeat
Table 14.2.2.3.3	Local Cutaneous Safety Evaluation by Treatment Group and Visit- Excluding Subjects with Signs or Symptoms at Baseline -Dryness	Safety	N/A	Repeat
Table 14.2.2.3.4	Local Cutaneous Safety Evaluation by Treatment Group and Visit- Excluding Subjects with Signs or Symptoms at Baseline -Burning	Safety	N/A	Repeat
Table 14.2.2.3.5	Local Cutaneous Safety Evaluation by Treatment Group and Visit- Excluding Subjects with Signs or Symptoms at Baseline -Stinging	Safety	N/A	Repeat
Table 14.2.2.3.6	Local Cutaneous Safety Evaluation by Treatment Group and Visit- Excluding Subjects with Signs or Symptoms at Baseline -Itching	Safety	N/A	Repeat

Display Number	Title	Populations	Subgroup	Unique/ Repeat
Safety Tables				
Table 14.3.1.1	Overall Summary of Treatment Emergent Adverse Events	Safety	N/A	Unique
Table 14.3.1.2	Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term	Safety	N/A	Unique
Table 14.3.1.2.1	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity	Safety	N/A	Repeat
Table 14.3.1.2.2	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug	Safety	N/A	Repeat
Table 14.3.1.2.3	Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Seriousness	Safety	N/A	Repeat
Table 14.3.1.3	Listing of Serious Adverse Events	Safety	N/A	Unique
Table 14.3.1.4	Listing of Adverse Events Leading to Discontinuation of Study Treatment	Safety	N/A	Repeat
Table 14.3.2	Summary of Physical Examination Results and Change from Baseline	Safety	N/A	Unique
Table 14.3.3	Summary of Vital Sign Results and Change from Baseline	Safety	N/A	Unique

Listings				
Display Number	**Title**	**Populations**	**Subgroup**	**Unique/ Repeat**
Listing 16.2.1.1	Subject Disposition	All Subjects	N/A	Unique
Listing 16.2.1.2	Study Visit Dates	All Subjects	N/A	Unique
Listing 16.2.2.1	Inclusion/Exclusion Criteria	All Subjects	N/A	Unique
Listing 16.2.2.2	Subject Eligibility	All Subjects	N/A	Unique
Listing 16.2.2.3	Protocol Deviations (PD)/Violations (PV)	All Subjects	N/A	Unique
Listing 16.2.3	Study Populations	All Subjects	N/A	Unique
Listing 16.2.4.1	Demographic and Baseline Characteristics	All Subjects	N/A	Unique
Listing 16.2.4.2	Medical History	All Subjects	N/A	Unique
Listing 16.2.4.3	Prior Medications	All Subjects	N/A	Unique
Listing 16.2.4.4	Concomitant Medications	All Subjects	N/A	Repeat
Listing 16.2.5.1	Study Drug Dispensing	All Subjects	N/A	Unique
Listing 16.2.5.2	Study Drug Record/Compliance	All Subjects	N/A	Unique
Listing 16.2.6.1	Investigator's Global Assessment (IGA) of the Face	All Subjects	N/A	Unique
Listing 16.2.7.1	Adverse Events by Subject, System Organ Class and Preferred Term	All Subjects	N/A	Unique
Listing 16.2.7.2	Adverse Events by System Organ Class, Preferred Term and Subject	All Subjects	N/A	Repeat
Listing 16.2.8.1	Urine Pregnancy Test Results	All Subjects	N/A	Unique
Listing 16.2.8.2	Vital Signs	All Subjects	N/A	Unique
Listing 16.2.8.3	Physical Examination Data	All Subjects	N/A	Unique
Listing 16.2.8.4.1	Local Cutaneous Tolerance Data of the Face	All Subjects	N/A	Unique
Listing 16.2.8.4.2.1	Lesion Counts of the Face	All Subjects	N/A	Unique
Listing 16.2.8.4.2.2	Lesion Counts of the Back, Chest, and Shoulders	All Subjects	N/A	Repeat

Listings				
Display Number	**Title**	**Populations**	**Subgroup**	**Unique/ Repeat**
Listing 16.2.8.4.3.1	Inflammatory Lesion Counts on the Face	All Subjects	N/A	Unique
Listing 16.2.8.4.3.1	Inflammatory Lesion Counts on the Back, Chest, and Shoulders	All Subjects	N/A	Repeat
Listing 16.2.8.4.4.1	Non-Inflammatory Lesion Counts on the Face	All Subjects	N/A	Unique
Listing 16.2.8.4.4.2	Non-Inflammatory Lesion Counts on the Back, Chest, and Shoulders	All Subjects	N/A	Repeat
Listing 16.2.8.4.5.1	Nodulocystic Lesion Counts on the Face	All Subjects	N/A	Unique
Listing 16.2.8.4.5.2	Nodulocystic Lesion Counts on the Back, Chest, and Shoulders	All Subjects	N/A	Repeat
Listing 16.2.8.4.6	Cardiff Acne Disability Index (CADI) Data	All Subjects	N/A	Unique

Figures				
	No figures.			

11.2. Layout of Tables

Table 14.1.1.1
Subject Enrollment and Disposition
All Subjects

	Statistics	DFD-03 Lotion	Tazorac, 0.1% Cream	Vehicle Lotion	Vehicle Cream	Total
All Subjects						
Screened	n					xx
Screen Failures	n					xx
Randomized	n	xx	xx	xx	xx	xx
Subjects Included in:						
ITT Population [1]	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
PP Population	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Safety Population	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Total Completed Study	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Total Discontinued Study	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Reason Discontinued [2]						
Subject decision/withdrawal of consent	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Protocol deviation	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject became pregnant	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Unrelated Adverse Event	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Lost to follow-up	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Investigator discretion	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Subject's treatment randomization was unblinded	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: ITT = Intent-to-Treat. PP = Per-Protocol.
[1] Percentage and all subsequent percentages based on the total number randomized, unless otherwise noted.
[2] Percentage based on the total number who discontinued study.

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Table 14.1.1.2
Subject Enrollment by Study Site
Enrolled Subjects

Study Site	Statistic	Randomized	ITT [1]	PP [1]	Safety [1]	Completed [1]	Discontinued [1]
001	n (%)	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
002	n (%)	xx	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc.							
Total:	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: ITT = Intent-to-Treat. PP = Per-Protocol.
[1] Percentage is based on number randomized.

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Table 14.1.2
Summary of Protocol Deviations (PD)/Violations (PV)
ITT Population

Type	Protocol Deviation/Violation	Statistics	DFD-03 Lotion	Tazorac, 0.1% Cream	Vehicle Lotion	Vehicle Cream	Total
Major	<Protocol Deviation/Violation 1>	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	<Protocol Deviation/Violation 2>	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	<Protocol Deviation/Violation 3>	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Minor	<Protocol Deviation/Violation 4>	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	<Protocol Deviation/Violation 5>	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	<Protocol Deviation/Violation 6>	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Program: T-xxx.sas Programer: xxx ddmmmyyyy

Table 14.1.3.1
Summary of Demographics and Baseline Characteristics
ITT Population

Parameter	Statistics	DFD-03 Lotion (n=xxx)	Tazorac, 0.1% Cream (n=xxx)	Vehicle Lotion (n=xxx)	Vehicle Cream (n=xxx)	Total (n=xxx)
Age at Base (Years)	n	xxx	xxx	xxx	xxx	xxx
	Mean (SD)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)	xx.x (xx.x)
	Median	xx.xx	xx.xx	xx.xx	xx.xx	xx.xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Age Group at Baseline						
9 – 16 Years	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
17-64 Years	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
≥ 65 Years	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Gender						
Male	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Female	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Race						
White	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Black or African American	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Asian	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
American Indian or Alaska Native	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Native Hawaiian or Other Pacific Islander	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Other	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Ethnicity						
Hispanic or Latino	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Non-Hispanic or Non-Latino Unknown	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Fitzpatrick Classification Scale						
I	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
II	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
III	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
IV	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
V	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
VI	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Percentages are based on the total number of subjects in each treatment group. Source

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Repeat for:
Table 14.1.3.2 Summary of Demographics and Baseline Characteristics by Treatment Group – PP Population
Table 14.1.3.3 Summary of Demographics and Baseline Characteristics by Treatment Group – Safety Population

Table 14.1.4
Summary of Study Drug Exposure and Compliance by Location
Safety Population

Parameter	Statistic	DFD-03 Lotion (n=xxx)	Tazorac, 0.1% Cream (n=xxx)	Vehicle Lotion (n=xxx)	Vehicle Cream (n=xxx)	Total (n=xxx)
Number of Applications	n	xxx	xxx	xxx	xxx	xxx
	Mean (SD)	xxx (xx.xx)	xxx (xx.xx)	xxx (xx.xx)	xxx (xx.xx)	xxx (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Days of Exposure [1]	n	xxx	xxx	xxx	xxx	xxx
	Mean (SD)	xxx (xx.xx)	xxx (xx.xx)	xxx (xx.xx)	xxx (xx.xx)	xxx (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Days of Exposure [1]						
< 28 Days	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
28 to 56 Days	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
57 to 84 Days	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
> 84 Days	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Compliance (%) [2]	n	xxx	xxx	xxx	xxx	xxx
	Mean (SD)	xxx (xx.xx)	xxx (xx.xx)	xxx (xx.xx)	xxx (xx.xx)	xxx (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Compliance (%) [3] Yes						
No	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Percentages are based on the total number of subjects in each treatment group.
[1] Days of Exposure = (stop date of study drug – start date of study drug) +1
[2] Compliance % = A/P x 100 where A = Total number of applications actually applied. P= Total number of applications for the respective evaluation period.
[3] A subject is considered compliant with the dosing regimen if the subject has applied at least 80% but no more than 120% of the expected applications for the respective evaluation period.

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Table 14.1.5
Summary of Prior Medications
Safety Population

WHO-DD ATC Class Level 1 WHO-DD ATC Class Level 2 WHO-DD Preferred Term	Statistic	DFD-03 Lotion (n-xxx)	Tazorac, 0.1% (n=xxx)	Vehicle Lotion (n-xxx)	Vehicle Cream (n=xxx)	Total (n=xxx)
Number of Subjects with at Least One Prior Medication	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Class Level 1	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Class Level 2	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Preferred Term 1	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Preferred Term 2 etc.	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Class Level 1	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Class Level 2	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Preferred Term 1	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Preferred Term 2 etc.	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)

Note: Percentages are based on the total number in each treatment group
Prior medications are defined as medications with stop dates occurring before the date of first administration of the study drug. Refer to Section 6.6 in the SAP for prior medication rules.
At each level (WHO-DD ATC Class Level 1, WHO-DD ATC Class Level 2, and Preferred Term) of summarization, a subject was counted once if the subject reported one or more medications.
The World Health Organization Drug Dictionary (WHO-DD) version March 2017 edition – C format was used.

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Programming Notes:
1. Sort WHO-DD ATC Class Level 1 and WHO-DD ATC Class Level 2 by Alphabetical Order.
2. With respect to the Total Column, sort Preferred Term within each WHO-DD ATC Class Level 2 by decreasing incidence.

Table 14.1.6
Summary of Concomitant Medications
Safety Population

WHO-DD ATC Class Level 1 WHO-DD ATC Class Level 2 WHO-DD Preferred Term	Statistic	DFD-03 Lotion (n-xxx)	Tazorac, 0.1% (n=xxx)	Vehicle Lotion (n-xxx)	Vehicle Cream (n=xxx)	Total (n=xxx)
Number of Subjects with at Least One Prior Medication	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Class Level 1	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Class Level 2	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Preferred Term 1	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Preferred Term 2 etc.	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Class Level 1	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Class Level 2	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Preferred Term 1	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)
WHO-DD ATC Preferred Term 2 etc.	n (%)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)	xx (xx.xx)

Note: Percentages are based on the total number in each treatment group
Concomitant medications are defined as medications with start dates occurring before, on, or after the date of first administration of the study drug and stopping after the first administration of study drug or continuing beyond that. Refer to Section 6.6 in the SAP for concomitant medication rules.
At each level (WHO-DD ATC Class Level 1, WHO-DD ATC Class Level 2, and Preferred Term) of summarization, a subject was counted once if the subject reported one or more medications.
The World Health Organization Drug Dictionary (WHO-DD) version March 2017 edition – C format was used

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Programming Notes:
1. Sort WHO-DD ATC Class Level 1 and WHO-DD ATC Class Level 2 by Alphabetical Order.
2. With respect to the Total Column, sort Preferred Term within each WHO-DD ATC Class Level 2 by decreasing incidence.

Table 14.2.1.1.1
Primary Analysis of Efficacy Endpoint Descriptive Statistics of IGA Success[1] Rate at Week 4[2],[3]
ITT Population

	Statistics	DFD-03 Lotion (n=xxx)	Tazorec, 0.1% (n=xxx)	Vehicle Lotion (n=xxx)	Vehicle Cream, (n=xxx)	Total (n=xxx)
Number of Subjects IGA Success at Week 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
IGA Score 0 (Clear)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
IGA Score 0 and at least 2 grade reduction from baseline	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
IGA Score 1 (almost clear)	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
IGA Score 1 and at least 2 grade reduction from baseline	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] IGA success is defined as an IGA score of 0 (Clear) or 1 (almost clear) with at least a 2-grade reduction from baseline.
[2] Missing IGA values will be imputed by LOCF.
[3] Efficacy data from termination visit will be assigned to the nearest corresponding scheduled visit that has been missed and carried forward to the subsequent visits

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Programming Notes:
1. For table 14.2.3.1.1.3.1, [2] Missing IGA values will be imputed using Multiple Imputation based on Logistic Regression
2. For the PP repeat of this table omit footnote [2]

Repeat for:
Table 14.2.1.1.2 Primary Analysis of Efficacy Endpoint Descriptive Statistics of IGA Success Rate at Week 8 – ITT Population
Table 14.2.1.1.3 1 Primary Analysis of Efficacy Endpoint Descriptive Statistics of IGA Success Rate at Week 12 with MI – ITT
Table 14.2.1.1.3 2 Primary Analysis of Efficacy Endpoint Descriptive Statistics of IGA Success Rate at Week 12 ITT Population
Table 14.2.1.1.4 Primary Analysis of Efficacy Endpoint Descriptive Statistics of IGA Success Rate at Week 4 – PP Population.
Table 14.2.1.1.5 Primary Analysis of Efficacy Endpoint Descriptive Statistics of IGA Success Rate at Week 8 – PP Population.
Table 14.2.1.1.6 Primary Analysis of Efficacy Endpoint Descriptive Statistics of IGA Success Rate at Week 12 – PP Population.

Table 14.2.1.2.1
Absolute Change from Baseline in Inflammatory and Non-Inflammatory Lesions Counts[1], [2] at the Week 4 Visit
ITT Population

	Statistic	DFD-03 Lotion (n=xxx)	Tazorac, 0.1% Cream (n=xxx)	Vehicle Lotion (n=xxx)	Vehicle Cream (n=xxx)	Total (n=xxx)
Number of Subjects Evaluated at Week 4 [1]	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Count Change Inflammatory Lesion Counts on Face	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	IQR	xx – xx	xx – xx	xx – xx	xx – xx	xx – xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Count Change Non-Inflammatory Lesion Counts on Face	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	IQR	xx – xx	xx – xx	xx – xx	xx – xx	xx – xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Count Change Inflammatory Lesion Counts on Chest, Back, and Shoulders	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	IQR	xx – xx	xx – xx	xx – xx	xx – xx	xx – xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Count Change Non-Inflammatory Lesion Counts on Chest, Back, and Shoulders	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	IQR	xx – xx	xx – xx	xx – xx	xx – xx	xx – xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

[1] Missing Lesion counts will be imputed by LOCF.
[2] Efficacy data from termination visit will be assigned to the nearest corresponding scheduled visit that has been missed and carried forward to the subsequent visits.

Program: T-xxx.sas Programmer: xxx ddmmyyyy

Programming Notes:
1. For the PP repeat of this table omit footnote [1]
2. For table 14.2.1.2.3.1, MI, repeat for each imputation and summary from MIANALYZE

Repeat for:
Table 14.2.1.2.2 Absolute Change from Baseline in Inflammatory and Non-Inflammatory Lesions Counts at the Week 8 visit – ITT Population
Table 14.2.1.2.3 Absolute Change from Baseline in Inflammatory and Non-Inflammatory Lesions Counts at the Week 12 visit – ITT Population
Table 14.2.1.2.3.1 Absolute Change from Baseline in Inflammatory and Non-Inflammatory Lesions Counts at the Week 12 visit with MI– ITT Population
Table 14.2.1.2.4 Absolute Change from Baseline in Inflammatory and Non-Inflammatory Lesions Counts at the Week 4 visit – PP Population

Table 14.2.1.2.5 Absolute Change from Baseline in Inflammatory and Non-Inflammatory Lesions Counts at the Week 8 visit – PP Population
Table 14.2.1.2.6 Absolute Change from Baseline in Inflammatory and Non-Inflammatory Lesions Counts at the Week 12 visit – PP Population

Table 14.2.1.3.1
Percent Change from Baseline to Week 4 in Inflammatory and Non-Inflammatory Lesion Counts[1],[2]
ITT Population

	Statistics	DFD-03 Lotion (n=xxx)	Tazorac, 0.1% Cream (n=xxx)	Vehicle Lotion (n=xxx)	Vehicle Cream (n=xxx)	Total n=xxx)
Number of Subjects Evaluated at Week 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Percent Change in Inflammatory Lesion Counts on Face	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	IQR	xx – xx	xx – xx	xx – xx	xx – xx	xx – xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Percent Change in Inflammatory Lesion Counts on Chest, Back, and Shoulders	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	IQR	xx – xx	xx – xx	xx – xx	xx – xx	xx – xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Percent Change in non-Inflammatory Lesion Counts on Face	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	IQR	xx – xx	xx – xx	xx – xx	xx – xx	xx – xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Percent Change in non-Inflammatory Lesion Counts on Chest, Back, and Shoulders	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	IQR	xx – xx	xx – xx	xx – xx	xx – xx	xx – xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

[1] Missing Inflammatory Lesion Counts will be imputed by LOCF.
[2] Efficacy data from termination visit will be assigned to the nearest corresponding scheduled visit that has been missed and carried forward to the subsequent visits

Program: T-xxx.sas Programmer: ddmmmyyyy

Programming Notes:
1. For the PP repeat of this table omit footnote [1]

Repeat for:
Table 14.2.1.3.2 Percent Change from Baseline to Week 8 in Inflammatory and non-Inflammatory Lesion Counts – ITT Population
Table 14.2.1.3.3 Percent Change from Baseline to Week 12 in Inflammatory and non-Inflammatory Lesion Counts – ITT Population
Table 14.2.1.3.4 Percent Change from Baseline to Week 4 in Inflammatory and non-Inflammatory Lesion Counts – PP Population
Table 14.2.1.3.5 Percent Change from Baseline to Week 8 in Inflammatory and non-Inflammatory Lesion Counts – PP Population
Table 14.2.1.3.6 Percent Change from Baseline to Week 12 in Inflammatory and non-Inflammatory Lesion Counts – PP Population

Table 14.2.1.4.1
Change from Baseline to Week 4 in Cardiff Acne Disability Index (CADI)[1]
ITT Population

	Statistics	DFD-03 Lotion (n=xxx)	Tazorac, 0.1% Cream (n=xxx)	Vehicle Lotion (n=xxx)	Vehicle Cream (n=xxx)	Total n=xxx)
Number of Subjects Evaluated at Week 4	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Change in CADI	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	IQR	xx – xx	xx – xx	xx – xx	xx – xx	xx – xx
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

[1] Efficacy data from termination visit will be assigned to the nearest corresponding scheduled visit that has been missed and carried forward to the subsequent visits

Program: T-xxx.sas Programmer: ddmmmyyyy

Repeat for:
Table 14.2.1.4.2 Change from Baseline to Week 8 in Cardiff Acne Disability Index (CADI) – ITT Population
Table 14.2.1.4.2 Change from Baseline to Week 12 in Cardiff Acne Disability Index (CADI) – ITT Population
Table 14.2.1.4.2 Change from Baseline to Week 4 in Cardiff Acne Disability Index (CADI) – PP Population
Table 14.2.1.4.2 Change from Baseline to Week 8 in Cardiff Acne Disability Index (CADI) – PP Population
Table 14.2.1.4.2 Change from Baseline to Week 12 in Cardiff Acne Disability Index (CADI) – PP Population

Table 14.2.2.1
Subject Compliance – Total Number of Applications, Number and Percentage of Subjects who are Compliant[1] for the baseline to Week 12 Evaluation Period
ITT Population

	Statistics	DFD-03 Lotion (n=xxx)	Tazorac, 0.1% (n=xxx)	Vehicle Lotion (n=xxx)	Vehicle Cream (n=xxx)	Total (n=xxx)
Total Number of Applications DI	Mean (SD)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Number (%) of Subjects Compliant	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

[1] Efficacy data from termination visit will be assigned to the nearest corresponding scheduled visit that has been missed and carried forward to the subsequent visits

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Table 14.2.2.2.1
Local Cutaneous Safety Evaluation by Treatment Group and Visit Non-Lesional Erythema
Safety Population

	DFD-03 Lotion (n=xxx)		Tazorac, 0.1% Cream (n=xxx)		Vehicle Lotion (n=xxx)		Vehicle Cream (n=xxx)	
Visit	Score	Severity	Score	Severity	Score	Severity	Score	Severity
Baseline	x	xxxx	x	xxxx	x	xxxx	x	xxxx
Screening	x	xxxx	x	xxxx	x	xxxx	x	xxxx
Week 4	x	xxxx	x	xxxx	x	xxxx	x	xxxx
Week 8	x	xxxx	x	xxxx	x	xxxx	x	xxxx
Week 12	x	xxxx	x	xxxx	x	xxxx	x	xxxx
Unscheduled	x	xxxx	x	xxxx	x	xxxx	x	xxxx

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Repeat for:
Table 14.2.2.2.2 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Peeling – Safety Population
Table 14.2.2.2.3 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Dryness – Safety Population
Table 14.2.2.2.4 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Burning – Safety Population
Table 14.2.2.2.5 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Stinging – Safety Population
Table 14.2.2.2.6 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Itching – Safety Population
Table 14.2.2.3.1 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Excluding Subjects with Signs or Symptoms at Baseline – Non-Lesional Erythema – Safety Population
Table 14.2.2.3.2 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Excluding Subjects with Signs or Symptoms at Baseline – Peeling – Safety Population
Table 14.2.2.3.3 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Excluding Subjects with Signs or Symptoms at Baseline – Dryness – Safety Population
Table 14.2.2.3.4 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Excluding Subjects with Signs or Symptoms at Baseline – Burning – Safety Population
Table 14.2.2.3.5 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Excluding Subjects with Signs or Symptoms at Baseline – Stinging – Safety Population
Table 14.2.2.3.6 Local Cutaneous Safety Evaluation by Treatment Group and Visit – Excluding Subjects with Signs or Symptoms at Baseline – Itching – Safety Population

Table 14.3.1.1
Overall Summary of Treatment Emergent Adverse Events
Safety Population

Parameter	Statistics	DFD-03 Lotion (n=xxx)	Tazorac,0.1% (n=xxx)	Vehicle Lotion (n=xxx)	Vehicle Cream (n=xxx)	Total (n=xxx)
Total Number of TEAEs	n	xx	xx	xx	xx	xx
Total Number of TESAEs	n	xx	xx	xx	xx	xx
Total Number of TEAESIs	n	xx	xx	xx	xx	xx
Number of Subjects with:						
At Least One TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One Related TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One Severe (Grade 3) TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One TEAE Leading to Treatment	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One TEAE Leading to Death	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One TESAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One Releated TESAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
At Least One TEAESI	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)

Note: Percentages are based on the total number of subjects in each treatment group.
A TEAE is defined as any AE which started on or after the first administration of study drug and includes those events started prior to the first administration of study drug but which worsened after the first administration of study drug.
Adverse Events were coded using MedDRA version 20.0

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Table 14.3.1.2
Summary of Treatment Emergent Adverse Events by System Organ Class and Preferred Term
Safety Population

System Organ Class Preferred Term	Statistics	DFD-03 Lotion (n=xxx)	Tazorac, 0.1% (n=xxx)	Vehicle Lotion (n=xxx)	Vehicle Cream (n=xxx)	Total (n=xxx)
Total Number of TEAEs	n	xx	xx	xx	xx	xx
Number of Subjects with at Least One TEAE	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
System Organ Class #1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #3	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Etc						
System Organ Class #2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #1	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #2	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
Preferred Term #3	n (%)	xx (xx.x)	xx (xx.x)	xx	xx	xx (xx.x)
etc.						

Note: Percentages are based on the total number of subjects in each treatment group.
A TEAE is defined as any AE which started on or after the first administration of study drug and include those events started prior to the first administration of study drug but which worsened after the first administration of study drug.
A subject with an event coding to the same System Organ Class (SOC) or Preferred Term (PT) on more than one occasion is only counted once for that SOC and PT.
Adverse events were coded using MedDRA version 20.0

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Repeat for:
Table 14.3.1.2.1 Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Severity
Table 14.3.1.2.2 Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Relationship to Study Drug
Table 14.3.1.2.3 Summary of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and Seriousness

Table 14.3.1.3
Listing of Serious Adverse Events
Safety Population

Subject	System Organ Class/ Preferred Term/ Ae Verbatim	Start Date [Study Day #] [1]	Stop Date [Study Day #] [1]	TEAE	In Trt Area	Severity	Relation to Study Product [2]	Action Taken With Study Product [3]	Action Taken With Subject [4]	Outcome [5]	SAE
xxxxxx	xxxxxxxxxx/ xxxxxxxxxx/ xxxxxxxxxx	DDMMMYYYY [xx]	DDMMMYYYY [xx]	Yes No	Yes No	Mild Moderate Severe	1 2 3 4	1 2 3 4 5 6	None Hosp Chg in CM Other	1 2 3 4 5	Yes

Note: AE = Adverse Event. TEAE = Treatment-Emergent Adverse Event. SAE = Serious Adverse Event.
Adverse events were coded using MedDRA version 20.0
[1] Study Day # is calculated from baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/ Baseline visit.
[2] 1 = Not Related. 2 = Possibly Related. 3 = Probably Related. 4 = Definitely Related.
[3] 1 = Dose Not Changed. 2 = Drug Interrupted. 3 = Drug Withdrawn. 4 = Dose Reduced. 5 = Dose Increased. 6 = Unknown.
[4] Chg in CM = Change in Concomitant Medication. Hosp = Hospitalization.
[5] 1 = Recovered/Resolved. 2 = Recovered/Resolved with Sequelae. 3 = Not Recovered/Not Resolved. 4 = Unknown. 5 = Fatal.

Program: T-xxx.sas Programmer: xxx ddmmmyy

Repeat for:
Table 14.3.1.4 Listing of Adverse Events Leading to Discontinuation of Study Treatment.

Table 14.3.2
Summary of Physical Examination Results and Change from Baseline
Safety Population.

Visit / Body System	Result	Statistics	DFD-03 Lotion (n=xxx)	Tazorac, 0.1% (n=xxx)	Vehicle Lotion (n=xxx)	Vehicle Cream (n=xxx)	Total (n=xxx)
Baseline/							
General Appearance	Normal	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal,	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	NCS Abnormal,	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	CS Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
H.E.E.N.T	Normal	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	Abnormal,	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	NCS Abnormal,	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
	CS Missing	n (%)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)	xx (xx.x)
etc.							

Note: Baseline is the last available assessment prior to time of first study drug administration
NCS = Not Clinically Significant. CS = Clinically Significant

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Programming Notes:
1. Display Visits in the following order: Baseline, Week 12, Change from Baseline
2. Display Body System in the following order:
   a. General Appearance
   b. H.E.E.N.T
   c. Chest/Lungs
   d. Heart
   e. Abdominal
   f. Lymph Nodes
   g. Skin
   h. Extremities
   i. Musculoskeletal
   j. Neurological
   k. Other

Table 14.3.4
Summary of Vital Signs Results and Change from Baseline
Safety Population

Parameter	Statistics	DFD-03 Lotion	Tazorac, 0.1%	Vehicle Lotion	Vehicle Cream	Total
<Vital Sign Parameter> (<unit>)						
Baseline	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 4	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Change from Baseline to Week 4	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 8	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Change from Baseline to Week 8	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Week 12	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx
Change from Baseline to Week 12	n	xx	xx	xx	xx	xx
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x	xx.x	xx.x
	Min, Max	xx, xx	xx, xx	xx, xx	xx, xx	xx, xx

Note: Baseline is the last available assessment prior to time of first study drug administration

Program: T-xxx.sas Programmer: xxx ddmmmyyyy

Listing 16.2.1.1
Subject Disposition

Treatment:
[Description]

Subject	Study Populations for Analyses	Completed Study	Date Completed or Date Discontinued	Reason Discontinued
xxxxxx	Safety	Yes	DDMMMYYYY	Screen Failure
	ITT	No		Withdrawal by Subject
	PP			Protocol Deviation
	None			Pregnancy
				Lack of Efficacy
				Worsening Condition
				Related Adverse Event
				Unrelated Adverse Event
				Lost to Follow-up
				Physician Decision
				Subject's Treatment Randomization Was Unblinded
				Other

Note: ITT = Intent-to-Treat. PP = Per-Protocol

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Programming Note:
1. For Study Populations for Analyses column, list all study populations where study population flag in ADSL = "Y".
   a. If SAFFL = "Y" then list Safety.
   b. If ITTFL = "Y" then list ITT.
   c. If PPROTFL = "Y" then list PP.
   d. If SAFFL = "N" and ITTFL = "N" and PPROTFL = "N" then list None only.

Listing 16.2.1.2
Study Visit Dates

Subject	Study Populations for Analyses	Visit 1 Screening Day -60 to 0 Date [Study Day #]	Visit 2 Baseline Day 1 Date [Study Day #]	Visit 3 Week 4 Day 28 (±5 days) Date [Study Day #]	Visit 4 Week 8 Day 56 (±5 days) Date [Study Day #]	Visit 5 Week 12 Day 84 (±5 days) Date [Study Day #]	Unscheduled Visit Date [Study Day #]
xxxxxx	None Safety ITT PP	DDMMMYYYY [xx]	DDMMMYYYY [xx]	DDMMMYYYY [xx]	DDMMMYYYY [xx]	DDMMMYYYY [xx]	DDMMMYYYY [xx]

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while day -1 was the day prior to the Visit 2/Baseline visit.

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Listing 16.2.2.1
Inclusion/Exclusion Criteria

Criteria	Number	Description
Inclusion	1	xxxxxxxxxxxxxxxxxxxxxxxxx.
	2	
	3	
	4	
	5	
	6	
	7	
	8	
	9	
	10	
	11	
	12	
Exclusion	1	xxxxxxxxxxxxxxxxxxxxxxxxx.
	2	
	3	
	4	
	5	
	6	
	7	
	8	
	9	
Program: L-xxx.sas	Programmer: xxx	ddmmmyyyy

Programming Notes: Inclusion Criteria –

1. Subject understands the study procedures, is willing to comply with the study procedures and required visits, and agrees to participate by giving written informed consent. Subjects under the legal age of consent must provide written assent and must have the written informed consent of their legal guardian.
2. Subject (or legal guardian) must be willing to authorize use and disclosure of protected health information collected for the study.
3. Subject must be at least 12 years of age.
   - At selected site(s), a total of approximately eight subjects 9-11 years of age will be enrolled into the 2 arms of DFD-03 lotion group (active and vehicle).
4. Female subjects must be having their menstrual period at the Baseline Visit (as reported by the subject), except for subjects using hormonal contraceptives that preclude menstrual periods, if the subject is premenarchal, is postmenopausal for at least 12 months prior to baseline, is surgically sterilized (i.e. tubal ligation) or if the subject is without a uterus and /or both ovaries.
5. A clinical diagnosis of facial acne vulgaris with an Investigator's Global Assessment (IGA) score of 2 (mild) to 3 (moderate) at Baseline.
   - At selected site(s), up to twelve subjects with acne lesions on the chest and/or back (including shoulders) in addition to those on the face will treat their back and/or chest (including shoulders) in addition to their face.
6. Inflammatory lesion count (papules and pustules) of at least 20 on the face, including the nose, at Baseline.
   - This criteria is not applicable to the 9-11 years age group as long as subjects have an IGA score of 2 (mild) to 3 (moderate) at Baseline.
7. Non-inflammatory lesion count (closed and open comedones) of at least 25 on the face, including the nose, at Baseline.

- This criteria is not applicable to the 9-11 years age group as long as subjects have an IGA score of 2 (mild) to 3 (moderate) at Baseline.

8. No more than 2 nodulocystic lesions on the face, including the nose, at Baseline.
9. Females, regardless of childbearing potential:
   a. Must have a negative urine pregnancy test at Screening and Baseline. Test must have a sensitivity of at least 25 mIU/mL for βhCG.
   b. If sexually active, must be on or use an acceptable method of birth control.

Acceptable methods of birth control include:

- hormonal methods* or intrauterine device in use ≥ 90 days prior to Baseline; or
- partner has had a vasectomy at least 90 days prior to Baseline; or
- barrier methods plus spermicide; or Essure® that has been in place for at least 3 months before the screening visit with radiograph confirmation of fallopian tube blockage.

  ***Hormonal methods:** If on hormonal contraceptives, must have been on the same hormonal contraceptive product for 3 months (90 days) prior to Baseline and continued on same method and dose throughout the duration of the study. If subject had used hormonal birth control and had stopped, this should have occurred more than 6 months prior to Baseline.

  Exception: Sexually inactive female subjects are not required to practice a reliable method of contraception and may be enrolled at the investigator's discretion provided that they are counseled to remain sexually inactive for the duration of the study and understand the possible risks involved in getting pregnant during the study. An abstinent female must agree that if she becomes sexually active during the study she will use an acceptable form of contraception such as a barrier method with spermicide. Females who are surgically sterilized [e.g. hysterectomy, bilateral tubal ligation, bilateral oophorectomy] at least 1 year prior to Baseline or have been postmenopausal for at least 1 year prior to Baseline are not required to practice a reliable method of contraception.

10. Subjects agree not to use any product on the face during the entire course of study except for non-medicated, investigator-approved cleanser, sunscreen, face wash, and make-up as instructed by the investigator. Subjects should continue to use these investigator approved products for the duration of the study and should avoid any changes in these consumer products.
11. Subjects must be willing to comply with sun avoidance measures for the face (as well as back/chest including shoulders, if applicable) including use of investigator-approved sunscreen and/or hats, have limited sun exposure time, and have no tanning bed use.
12. Subject must be in good general health as determined by the investigator and supported by the medical history, physical examination, and normal or not clinically significant abnormal vital signs (blood pressure and pulse). Subjects are eligible if:
    - Systolic blood pressure (BP) < 160 and > 85 mmHg
    - Diastolic BP < 100 and > 50 mmHg
    - Pulse 50 to 100 bpm inclusive for adults; up to 110 bpm for subjects < 18years of age;

Exclusion Criteria

1. Females who are pregnant or lactating or planning to become pregnant during the study period.
2. Treatment with the following products:
   a. Topical acne treatments (retinoids, antibiotics, benzoyl peroxide, azelaic acid, resorcinol, salicylates, α-hydroxy/glycolic acid), or other topical facial medication (antifungals, steroids, anti-inflammatories) on the treatment area in the 14 days prior to the Baseline Visit, including prescription and non-prescription products.
   b. Systemic corticosteroids, systemic acne treatments including systemic antibiotics used for treatment of acne, photosensitizing agents (thiazides, phenothiazines), spironolactone, flutamide, or immunosuppressant drugs in the 30 days prior to the Baseline Visit.
   c. Systemic retinoid use (including high dose vitamin A > 10,000 units per day) in the 180 days prior to the Baseline Visit.
   d. Undertaken certain facial procedures such as chemical peel, laser treatment, photodynamic therapy, acne surgery, cryodestruction or chemodestruction, x-ray therapy, intralesional steroids, dermabrasion, or depilation (except eyebrow shaping) in the 30 days prior to Baseline visit. After the subject is enrolled in the study, eyebrow shaping (except for tweezing) will also be prohibited.
   e. Treatment with a medication or procedure that, in the opinion of the investigator, would put the subject at unacceptable risk for participation in the study or may interfere with evaluations in the study.

f. Treatment with an investigational product or device in the 30 days prior to the Baseline Visit.

3. Known allergic reaction to retinoids or tazarotene or any of the other ingredients of these products. The inactive ingredients are sodium lauryl sulphate, stearyl alcohol, cetyl alcohol, gluconolactone, Vitamin E polyethylene glycol succinate, glycerin, carbomer P 971, propylparaben, methylparaben, edetate disodium, butylated hydroxytoluene, medium-chain triglyceride, trolamine, and purified water.
4. Presence of any facial skin disease or condition that would interfere with the study or place the subject at unacceptable risk including sunburn, rosacea, seborrheic dermatitis, perioral dermatitis, lupus, dermatomyositis, psoriasis, eczema, squamous cell carcinoma, acneiform eruptions caused by medications, steroid acne, steroid folliculitis, bacterial folliculitis or any other facial disease or condition.
5. Excessive facial hair (i.e., heavy beard or mustache), facial tattoos or facial disfigurement that would interfere with study assessments.
6. Subjects with a serious and/or chronic medical condition such as chronic or active liver disease, renal impairment, heart disease, severe respiratory disease, rheumatoid arthritis, current malignancies, immunocompromised conditions, or any other disease that, in the opinion of the investigator, would interfere with the study or place the subject at unacceptable risk.
7. Subjects who have been treated for alcohol dependence or alcohol or drug abuse in the year prior to the Baseline Visit.
8. Subjects who have been in another investigational trial within 30 days of the Baseline Visit.
9. Subjects may not have a personal relationship with any member of the study staff or be part of the staff at the medical practice.

Listing 16.2.2.2
Subject Eligibility

Subject	Study Populations for Analyses	Met All Entrance Criteria	If No, List of Inclusion/Exclusion Violations	Subject Randomized
xxxxxx	None Safety ITT PP	Yes No	I3, I4, E2	Yes No

Note: ITT = Intent-to-Treat. PP = Per-Protocol

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Listing 16.2.2.3
Protocol Deviations (PD)/Violations (PV)

Subject	Study Populations for Analyses	Protocol Deviation/Violation	Major/Minor	Is Subject Excluded from Any Planned Analyses Population Due to PD/PV
xxxxxx	None Safety ITT PP	xxxxxxxxxxxxxxxxxxxxxxx	Major Minor	Yes No

Note: ITT = Intent-to-Treat. PP = Per-Protocol

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Listing 16.2.3
Study Populations

		Safety Population [1]		ITT Population [2]		PP Population [3]	
Subject	Study Populations for Analyses	Included	Reason Excluded	Included	Reason Excluded	Included	Reason Excluded
xxxxxx	None Safety ITT PP	Yes No	xxxxxxxxxxxxxxxxxxxxx.	Yes No	xxxxxxxxxxxxxxxxxxxxx.	Yes No	xxxxxxxxxxxxxxxxxxxxx.

Note: ITT = Intent-to-Treat. PP = Per-Protocol
[1] All subjects who received at least one confirmed dose of study product and provided any post baseline safety information were included in the safety population
[2] The ITT population is the primary efficacy analysis data set and consists of all subjects who were randomized and dispensed study medication.
[3] The PP population included all subjects in the ITT population who completed the Week 12 evaluation without any major protocol violations

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Programming Notes:

1. For Study Populations for Analyses column, list all study populations where study population flag in ADSL = "Y":
   a. If SAFFL = "Y" then list Safety.
   b. If ITTFL = "Y" then list ITT.
   c. If PPROTFL = "Y" then list PP.
   d. If SAFFL = "N" and ITTFL = "N" and PPROTFL = "N" then list None only.
2. If subject is a Screen Failure, then reason excluded from all study populations is "Screen Failure".
3. If subject is not a Screen Failure and SAFFL = "N" and TR01SDT is missing then reason excluded from safety population is "No confirmed dose of study drug.".
4. If subject is not a Screen Failure and SAFFL = "N" and TR01SDT is not missing then reason excluded from safety population is "No post baseline safety data.".
5. If subject is not a Screen Failure and ITTFL = "N" then reason excluded from ITT population is "Not randomized and dispensed study drug.".
6. If subject is not a Screen Failure and PPROTFL = "Y" and ITTFL = "N" then reason excluded from PP population is "Not in ITT population.".
7. If subject is not a Screen Failure and PPROTFL = "Y" and ITTFL = "Y" then reason excluded from PP population is "Did not complete Week 12 evaluation without any major protocol violations.".

Listing 16.2.4.1
Demographics and Baseline Characteristics

Subject	Study Populations for Analyses	Age	Gender	Race	Ethnicity	IGA Scale at Baseline [1]	Fitzpatrick Skin Type Classification Scale at Baseline [2]
xxxxxx	None	xx	Male	White	Hispanic or Latino	0	I
	Safety		Female	Black or African American Asian	Non-Hispanic or Non-Latino	1	II
	ITT			American Indian or Alaska Native	Unknown	2	III
	PP			Native Hawaiian or Other Pacific Islander		3	IV
				Other		4	V
							VI

Note: ITT = Intent-to-Treat. PP = Per-Protocol
[1] 0 = Clear; 1 = Almost Clear; 2 = Mild; 3 = Moderate; 4 = Severe
[2] I = White; Very Fair; Red or Blond Hair; Blue Eyes; Freckles. II = White; Fair; Red or Blond Hair, Hazel or Green Eyes. III = Cream White; Fair with Any Eye or Hair Color. IV = Brown; Typical Mediterranean Caucasian Skin. V = Brown; Mid-Eastern Skin Types. VI = Black.

Program: L-xxx .sas Programmer: xxx ddmmmyyyy

Listing 16.2.4.2
Medical History

Subject	Study Population for Analyses	Medical History Category / Reported Term	Onset Date	Ongoing	Concomitant Medication
xxxxxx	None	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx/	DDMMMYYYY	Yes	Yes
	Safety	xxxxxxxxxxxxxxxxxxxxxxxxxxxxxx		No	No
	ITT				
	PP				

Note: ITT = Intent-to-Treat. PP = Per-Protocol

Program: L-xxx. sas Programmer: xxx ddmmmyyyy

Listing 16.2.4.3
Prior Medications

Subject	Study Population for Analyses	WHO-DD ATC Class Level 1/ WHO-DD ATC Class Level 2/ WHO-DD Preferred Term/ Prior Medication Verbatim/ Indication	Start Date	End Date	Ongoing
xxxxxx	None	xxxxxxxxxxxxxxxxxxxxxx/	DDMMMYYYY	DDMMMYYYY	Yes
	Safety	xxxxxxxxxxxxxxxxxxxxxx/			No
	ITT	xxxxxxxxxxxxxxxxxxxxxx/			
	PP	xxxxxxxxxxxxxxxxxxxxxx/			
		xxxxxxxxxxxxxxxxxxxxxx			

Note: ITT = Intent-to-Treat. PP = Per-Protocol
Prior Medications were defined as medications with stop dates occurring before the date of first administration of the study drug. Refer to Table 17 in the SAP for prior medication rules.
The World Health Organization Drug Dictionary (WHO-DD) version March 2017 edition – C format was used to code prior medications.

Program: L-xxx .sas Programmer: xxx ddmmmyyyy

Repeat for:
Listing 16.2.4.4 Concomitant Medications

Listing 16.2.5.1
Study Drug Dispensing

Subject	Study Populations for Analyses	Bottle ID	Dispensed Date	Dispensed Weight (g)	Returned Date	Returned Weight (g)	Dispensed/Assessed By (Initials)
xxxxxx	None Safety ITT	xxxxx	DDMMMYYYY	xx	DDMMMYYYY	xx	XXX

Note: ITT = Intent-to-Treat. PP = Per-Protocol.

Program: L-xxx.sas
Programmer: xxx
ddmmmyyyy

Listing 16.2.5.2
Study Drug Record/Compliance

		First Day of Application		Last Day of Application				
Subject	Study Populations for Analyses	Date	No. of Doses Applied	Date	No. of Doses Applied	Total No. of Application Applied	Total No. Of Applications Missed	If Lost to Follow-up, Was at Least One Dose Applied?
xxxxxx	None Safety ITT PP	DDMMMYYYY	xxx	DDMMMYYYY	xxx	xxx	xxx	Yes No

Note: ITT = Intent-to-Treat. PP = Per-Protocol.
Total No. of Applications Applied/Missed was obtained from the treatment record page of eCRF

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

ddmmmyyyy

Listing 16.2.6.1
Investigator's Global Assessment (IGA) of the Face

Subject	Study Populations for Analyses	Visit	Date [Study Day #]	Was IGA Assessment Performed?	IGA Assessment of Subjects Overall Acne Vulgaris Condition [1]	Investigator's Initials
xxxxx	None	Screening	DDMMMYYYY	Yes	0	XXX
	Safety	Baseline	[xx]	No	1	
	ITT	Week 4			2	
		Week 8				
		Week 12				

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/ Baseline visit.
[1] 0 = Clear. 1 = Almost Clear. 2 = Mild. 3 = Moderate. 4 = Severe.

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Listing 16.2.7.1
Adverse Events by Subject, System Organ Class and Preferred Term

Subject / Study Pop	System Organ Class/ Preferred Term/ AE Verbatim	Start Date [Study Day #] [1]	Stop Date [Study Day #] [1]	TEAE	In Trt Area	Severity	Relation to Study Product [2]	Action Taken With Study Product [3]	Action Taken With Subject [4]	Outcome [5]	SAE
xxxxxx / None Safety ITT PP	xxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxx/ xxxxxxxxxxxxxxx	DDMMMYYYY	DDMMMYYYY	Yes No	Yes No	Mild Moderate Severe	1 2 3 4 5	1 2 3 4	None Hosp Chg in CM Other	1 2 3 4 5	Yes No

Note: AE = Adverse Event. TEAE = Treatment-Emergent Adverse Event. SAE= Serious Adverse Event. Adverse events were coded using MedDRA version 20.0.
[1] Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/ Baseline visit.
[2] 1 = Not Related. 2 = Possibly Related. 3 = Probably Related. 4 = Definitiely Related.
[3] 1 = Dose Not Changed. 2 = Drug Interrupted. 3 = Drug Withdrawn. 4 = Dose Reduced. 5 = Dose Increased. 6 = Unknown.
[4] Chg in CM = Change in Concomitant Medication. Hosp = Hospitalization.
[5] 1 = Recovered/Resolved. 2 = Recovered/Resolved with Sequelae. 3 = Not Recovered/Not Resolved. 4 = Unknown. 5 = Fatal.

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Repeat for:
Listing 16.2.7.2 Adverse Events by System Organ Class, Preferred Term and Subject

Listing 16.2.8.1
Urine Pregnancy Test Results

Subject	Populations for Analyses	Visit	Date [Study Day #]	Was the pregnancy test	Result
xxxxxx	None	Screening	DDMMMYYYY	Yes	Positive
	Safety	Baseline	[xx]	No	Negative
	ITT	Week 4			
	PP	Week 8			
		Week 12			
		Unscheduled			

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/ Baseline visit.

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Programming Note:
1. Within subject sort by date.

Listing 16.2.8.2
Vital Signs

Subject	Populations for Analyses	Parameter	Visit	Date [Study Day #]	Position	Done	Result	Unit	If out of range, Not Clinically Significant?
xxxxxx	None	Height	Screening	DDMMMYYYY	xxxxxx	Yes	xxx.x	in	Yes
	Safety	Weight	Baseline			No	xxx.x	lb	No
	ITT	Systolic Blood Pressure	Week 4				xxx	mmHg	
	PP	Diastolic Blood Pressure	Week 8				xxx	mmHg	
		Pulse Rate	Week 12				xxx	bpm	

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/ Baseline visit.

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Programming Note:
1. Within parameter sort by date.

Listing 16.2.3
Physical Examination Data

Subject	Populations for Analyses	Visit	Was a Complete Physical Exam Performed at this visit?	Did physical exam result in any abnormalities?	Body System	Describe Abnormalities Using Standard Medical Nomenclature	Clinically Significant?
xxxxxx	None	Baseline	Yes	Yes	General Appearance	xxxxxxxxxxxxxx	NCS
	Safety		No	No	H.E.E.N.T		CS
	ITT				Chest/Lungs		
	PP				Heart		
					Abdominal		
					Lymph Nodes Skin		
					Extremities		
					Musculoskeletal		
					Neurological		
					Other = <PESPEC>		

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2 / Baseline visit.
NCS = Not Clinically Significant. CS = Clinically Significant.

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Programming Note:
1. If Body System = Other then list PESPEC instead.

Listing 16.2.8.4.1
Local Cutaneous Tolerance Data of the Face

Subject	Study Population for Analyses	Parameter	Visit	Date [Study Day #]	Was Local Cutaneous Tolerance signs and symptoms performed?	Score	Severity	Investigator's Initials
xxxxxx	None	Non-Lesional Erythema	Screening	DDMMMYYYY	Yes	0	None	XXX
	Safety	Peeling	Baseline	[xx]	No	1	Mild	
	ITT	Dryness	Week 4			2	Moderate	
	PP	Stinging	Week 8			3	Severe	
		Burning	Week 12					
		Itching	Unscheduled					

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/ Baseline visit.

Program: L-xxx .sas | Programmer: xxx | ddmmmyyyy

Programming Note:
1. Within Parameters sort by date.

Listing 16.2.8.4.2.1
Lesion Counts of the Face

Subject	Study Populations for Analyses	Visit	Date [Study Day #]	Was Lesion Counts Performed?	Lesion Category	Count	Investigator's Initials
xxxxxx	None	Screening	DDMMMYYYY	Yes	Total Inflammatory	xx	XXX
	ITT	Baseline	[xx]	No	Total Non-Inflammatory		
	PP	Week 4			Total Nudulocystic Lesion		
		Week 8					
		Week 12					
		Unscheduled					

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/Baseline visit.

Program: L-xxx.sas Program: xxx ddmmmyyyy

Repeat for:
Listing 16.2.8.4.2.2 Lesion Counts of the Chest, Back, and Shoulders

Listing 16.2.8.4.3.1
Inflammatory Lesion Counts of the Face

Subject	Study Populations for Analyses	Visit	Date [Study Day #]	Was Lesion Counts Performed?	Lesion Category	Count	Investigator's Initials
xxxxxx	None	Screening	DDMMMYYYY	Yes	Papules	xx	XXX
	ITT	Baseline	[xx]	No	Pustules		
	PP	Week 4					
		Week 8					
		Week 12					
		Unscheduled					

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/Baseline visit.

Program: L-xxx.sas Program: xxx ddmmmyyyy

Repeat for:
Listing 16.2.8.4.3.2 Inflammatory Lesion Counts of the Chest, Back, and Shoulders

Listing 16.2.8.4.4.1
Non-Inflammatory Lesion Counts of the Face

Subject	Study Populations for Analyses	Visit	Date [Study Day #]	Was Lesion Counts Performed?	Lesion Category	Count	Investigator's Initials
xxxxxx	None	Screening	DDMMMYYYY	Yes	Open Comedones	xx	XXX
	ITT	Baseline	[xx]	No	Close Comedones		
	PP	Week 4					
		Week 8					
		Week 12					
		Unscheduled					

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/Baseline visit.

Program: L-xxx.sas Program: xxx ddmmmyyyy

Repeat for:
Listing 16.2.8.4.4.2 Non-Inflammatory Lesion Counts of the Chest, Back, and Shoulders

Listing 16.2.8.4.5.1
Nodulocystic Lesion Counts of the Face

Subject	Study Populations for Analyses	Visit	Date [Study Day #]	Was Lesion Counts Performed?	Lesion Category	Count	Investigator's Initials
xxxxxx	None	Screening	DDMMMYYYY	Yes	Nodules	xx	XXX
	ITT	Baseline	[xx]	No	Cysts		
	PP	Week 4					
		Week 8					
		Week 12					
		Unscheduled					

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/Baseline visit.

Program: L-xxx.sas Program: xxx ddmmmyyyy

Repeat for:
Listing 16.2.8.4.5.2 Nodulocystic Lesion Counts of the Chest, Back, and Shoulders

Listing 16.2.8.4.6
Cardiff Acne Disability Index (CADI) Data

Subject	Populations for Analyses	Visit	Date [Study Day #]	Question Number	Question: During the last month:	Score	Severity
xxxxxx	None Safety ITT PP	Baseline Week 4 Week 8 Week 12 Unscheduled	DDMMMYYYY [xx]	1 2 3 4 5 Total	xxxxxxxxxxxxxxx	0 1 2 3 xx	xxxxxxxxxx

Note: Study Day # is calculated from the baseline (Visit 2) date. Day 1 was the baseline date while Day -1 was the day prior to the Visit 2/ Baseline visit. The CADI score was calculated by summing the score of each question resulting in a possible maximum of 15 and a minimum of 0. The higher the score, the more the quality of life was impaired.

Program: L-xxx.sas Programmer: xxx ddmmmyyyy

Programming Notes:
1. Within subject sort by date.
2. Insert a blank row after each visit.
3. Insert a blank row after each question.

Questions were:
1. As a result of having acne, have you been aggressive, frustrated or embarrassed? Severity categories were: a. Very much indeed. Score = 3.
   b. A lot. Score = 2.
   c. A little. Score = 1.
   d. Not at all. Score = 0.
2. Do you think that having acne interfered with your daily social life, social events or relationships with members of the opposite sex? Severity categories were:
   a. Severely, affecting all activities. Score = 3.
   b. Moderately, in most activities. Score = 2.
   c. Occasionally or in only some activities. Score = 1.
   d. Not at all. Score = 0.
3. Have you avoided public changing facilities or wearing swimming costumes because of your acne? Severity categories were:
   a. All of the time. Score = 3.
   b. Most of the time. Score = 2.
   c. Occasionally. Score = 1.
   d. Not at all. Score = 0.

4. How would you describe your feelings about the appearance of your skin? Severity categories were:
   a. Very depressed and miserable. Score = 3.
   b. Usually concerned. Score = 2.
   c. Occasionally concerned. Score = 1.
   d. Not bothered. Score = 0.
5. Please indicate how bad you think your acne is now:
   a. The worst it could possibly be. Score = 3.
   b. A major problem. Score = 2.
   c. A minor problem. Score = 1.
   d. Not a problem. Score = 0.