STATISTICAL ANALYSIS PLAN

AMENDMENT 3

Study: DV0002

Product: Bimekizumab

NORTH AMERICAN SUBSTUDY TO PS0014

A MULTICENTER, RANDOMIZED, OPEN-LABEL STUDY TO EVALUATE THE SAFE AND EFFECTIVE USE OF THE PREFILLED SAFETY SYRINGES OR THE AUTO-INJECTOR FOR THE SUBCUTANEOUS SELF-INJECTION OF BIMEKIZUMAB SOLUTION BY SUBJECTS WITH MODERATE TO SEVERE CRONIC PLAQUE PSORIASIS

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LIST OF ABBREVIATIONS

ADE	adverse device effect
AE	adverse event
bimekizumab-AI-1mL	1mL bimekizumab auto-injector
bimekizumab-AI-2mL	2mL bimekizumab auto-injector
bimekizumab-SS-1mL	1mL bimekizumab safety syringe
bimekizumab-SS-2mL	2mL bimekizumab safety syringe
BKZ	bimekizumab
BMI	body mass index
COVID-19	Coronavirus Disease 2019
ES	Enrolled Set
FAS	Full Analysis Set
FAS-a	Full Analysis Set for the bimekizumab-AI-1mL Full Analysis Set for the bimekizumab AI 2mL
FAS-s	Full Analysis Set for the bimekizumab-SS-1mL Full Analysis Set for the bimekizumab SS 2mL
HLT	higher level term
IFU	instructions for use
IMP	investigational medicinal product
LLOQ	lower level of quantification
MedDRA	Medical Dictionary for Regulatory Activities
PFS	prefilled syringe
PK	pharmacokinetic(s)
PK-PPS	Pharmacokinetic Per Protocol Set

PK-PPS-a	Pharmacokinetic Per Protocol Set for the bimekizumab-AI-1mL Pharmacokinetic Per Protocol Set for the bimekizumab-AI-2mL
PK-PPS-s	Pharmacokinetic Per Protocol Set for the bimekizumab-SS-1mL Pharmacokinetic Per Protocol Set for the bimekizumab-SS-2mL
PEOT	Premature End of Treatment
PSO	psoriasis
PT	preferred term
Q4W	every 4 weeks
Q8W	every 8 weeks
SADE	serious adverse device effect
SAE	serious adverse event
SAP	Statistical Analysis Plan
sc	subcutaneously
SIAQ	Self-Injection Assessment Questionnaire
SD	standard deviation
SFU	Safety Follow-Up
SOC	System Organ Class
SS	Safety Set
SS-a	Safety Set for the bimekizumab-AI-1mL Safety Set for the bimekizumab AI 2mL
SS-s	Safety Set for the bimekizumab-SS-1mL Safety Set for the bimekizumab SS 2mL
TEADE	treatment-emergent adverse device effect
TEAE	treatment-emergent adverse event

VAS	visual analog scale
WHO	World Health Organization

1 INTRODUCTION

This statistical analysis plan (SAP) defines the scope of the statistical analyses and provides a detailed description of the statistical methodology for subject data obtained in this substudy of PS0014. The SAP is based on the following study document:

- Final Protocol DV0002, 26 Jul 2018.
- Protocol amendment 1, 28 Oct 2019.

All references to study protocol hereafter refer to this version of the protocol.

All analyses will be performed separately for the 1mL device cohort and for the 2mL device cohort. Once subjects in the 1mL device cohort complete DV0002, a final analysis will be performed for that cohort, and a clinical study report will be prepared. A separate final analysis will be performed for the 2mL device cohort once all data have been collected and will be reported separately from the initial clinical study report.

2 PROTOCOL SUMMARY

2.1 Study objectives

2.1.1 Primary objective

The primary objective of the study is to evaluate for each device the ability of subjects with moderate to severe chronic plaque psoriasis (PSO) to safely and effectively self-inject bimekizumab 8 weeks after training in the self-injection technique.

2.1.2 Secondary objective

The secondary objective of the study is to evaluate, for each device, the ability of subjects with moderate to severe chronic plaque PSO to safely and effectively self-inject bimekizumab immediately after training in the self-injection technique.

2.1.3 Other objectives

Other objectives of the study are to evaluate the following:

- Subject experience of self-injection using the investigational devices as assessed by the pain visual analog scale (VAS) and the Self-injection Assessment Questionnaire (SIAQ).
- Trough pharmacokinetic (PK) (trough bimekizumab) levels associated with self-injection using the investigational devices, injection by study personnel, injection site (abdomen or thigh), and body mass index (BMI) category (by tertile).
- The structural and mechanical integrity of the investigational devices after completion of self-injection.
- The overall safety and tolerability of self-injections using the investigational devices.

2.2 Study variables

2.2.1 Primary outcome variable

The primary outcome variable is the percentage of subjects able to self-administer safe and effective injections using the 1mL bimekizumab safety syringe (bimekizumab-SS-1mL), 1mL bimekizumab auto-injector (bimekizumab-AI-1mL), 2mL bimekizumab safety syringe

(bimekizumab SS 2mL), or 2mL bimekizumab auto-injector (bimekizumab-AI-2mL), 8 weeks after training in self-injection technique. Safe and effective self-injection will be evaluated by the study personnel and is
defined as:

- Complete dose delivery: Subject self-injects the complete dose of bimekizumab as confirmed by a visual inspection of the device which shows that the investigational medicinal product (IMP) is delivered completely (ie, container is empty), and
- No adverse device effects (ADEs) that would preclude continued use of the device for self-injection (ie, no serious adverse device effects (SADEs) and/or ADEs leading to withdrawal from the DV0002 substudy).

In the DV0002 substudy, for the 1mL devices the 320mg bimekizumab dose will be administered as two 160mg injections with either 2 bimekizumab-SS-1mL devices or 2 bimekizumab-AI-1mL devices. Each self-injection will be evaluated for safety and effectiveness by study personnel using the above criteria. The endpoint of safe and effective self-injection will be met only if both self-injections are determined to be safe and effective.

For the 2ml devices, the 320mg bimekizumab dose will be administered as 1 injection with either 1 bimekizumab-SS-2mL or 1 bimekizumab-AI-2mL device. Each self-injection will be evaluated for safety and effectiveness by study personnel using the above criteria. The endpoint of safe and effective self-injection will be met if the single self-injection is determined to be safe and effective.

2.2.2 Secondary outcome variable

The secondary outcome variable is the percentage of subjects able to self-administer safe and effective injections using the bimekizumab-SS-1mL, bimekizumab-AI-1mL bimekizumab SS 2mL, or 1 bimekizumab-AI-2mL at DV0002 Baseline (the first self-injection visit, immediately after training in self-injection technique). Safe and effective self-injection will be evaluated by study personnel and is defined as for the primary outcome variable (see Section 2.2.1).

2.2.3 Other variables

2.2.3.1 Outcome variables

The other outcome variables are:

- Responses to pre-injection SIAQ (versions 2.0 and 2.1) at DV0002 Baseline.

  Whenever SIAQ is assessed, version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL and bimekizumab-SS-2mL and version 2.1 of the SIAQ will be used to assess bimekizumab-AI-1mL and bimekizumab AI 2mL.
- Responses to post-injection SIAQ (versions 2.0 for bimekizumab-SS-1ml and 2.1 for bimekizumab-1ml-AI) by visit following self-injection using the assigned device at DV0002 Baseline and Week 8.
- Injection site pain (using a VAS; 100mm) by visit after self-injection using the assigned device at DV0002 Baseline and Week 8.

- Percentage of used devices identified as having structural or mechanical integrity issues after completion of self-injection. This is based on a visual examination of the device that shows clear evidence of damage and/or compromised structural or mechanical integrity.

2.2.3.2 Pharmacokinetic variable

The PK variable is trough PK (bimekizumab) levels associated with self-injection using the investigational device, injection by study personnel, injection site (abdomen or thigh), and BMI category (by tertile). Trough levels will be assessed at DV0002 Baseline, Week 4, Week 8, and Week 12 for subjects who receive bimekizumab Q4W and trough levels will be assessed at DV0002 Baseline, Week 8, and Week 16 for subjects who receive bimekizumab Q8W.

2.2.3.3 Safety variable

The other safety variable is the occurrence of ADEs. An ADE is an adverse event (AE) related to the use of an investigational device. An ADE must meet 1 or more of the following criteria:

- Adverse event resulting from insufficiencies or inadequacies in the instructions for use (IFU), the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device.
- Adverse event that is a result of a use error or intentional misuse of the investigational device.

Additional safety and tolerability variables will be collected as described in the PS0014 study protocol.

2.3 Study design and conduct

2.3.1 Study description

DV0002 is a Phase 3 open-label, randomized, noncomparator, North America-only substudy to PS0014. PS0014 will evaluate the long-term safety, tolerability, and efficacy of bimekizumab in subjects with moderate to severe chronic plaque PSO; study personnel will administer bimekizumab to subjects in a 1mL PFS.

In the DV0002 substudy, the safe and effective use of the bimekizumab-SS-1mL, bimekizumab-AI-1mL, bimekizumab-SS-2mL, or the bimekizumab-AI-2mL for the sc self-injection of bimekizumab by subjects with PSO will be evaluated.

Subjects from selected sites in the PS0014 feeder studies PS0008, PS0009, and PS0013 will be eligible for the DV0002 substudy. At DV0002 Baseline, each subject will be provided with training in self-injection and will receive the IFU and any other applicable training materials.

For the 1mL device cohort, subjects in the DV0002 substudy will perform self-injections at DV0002 Baseline (corresponding to the Baseline Visit of PS0014) with a subsequent self-injection at DV0002 Week 8 (corresponding to Week 8 of PS0014).

To allow flexible enrollment, subjects may be randomized in the 2mL device cohort at the PS0014 Week 24, Week 28, or Week 32 visit for subjects receiving bimekizumab Q4W or the PS0014 Week 24 or Week 32 visit for subjects receiving bimekizumab Q8W.

For the 2mL device cohort, subjects will perform self-injections at DV0002 Baseline with a subsequent self-injection 8 weeks after training. The 2mL device cohort will evaluate 2 self-injection devices: the bimekizumab SS 2mL and the bimekizumab AI 2mL.

2.3.2 Treatment Period

During the 16-week Treatment Period of DV0002, subjects will receive either bimekizumab 320mg Q8W or bimekizumab 320mg Q4W, based on their assigned dose at PS0014 Baseline. Baseline for DV0002 and Baseline for PS0014 will occur at the same time for the 1mL device cohort. In the 2mL device cohort, Baseline for DV0002 will occur at the PS0014 Week 24, Week 28, or Week 32 visit for subjects receiving bimekizumab Q4W or the PS0014 Week 24 or Week 32 visit for subjects receiving bimekizumab Q8W.

Eligible subjects (PS0014 entry criteria and DV0002 entry criteria) will be randomly assigned in a 1:1 ratio to perform self-injection using either the bimekizumab-SS-1mL or the bimekizumab-AI-1mL for the 1mL device cohort or using either the bimekizumab-SS-2mL or the bimekizumab-AI-2mL for the 2mL device cohort. Regardless of the assigned dose regimen, subjects will perform self-injection with the assigned device only at DV0002 Baseline and at DV0002 Week 8. For subjects in the bimekizumab 320mg Q4W dosing arm, injections will be administered by study personnel using the investigational device at Week 4 and Week 12; for subjects in both dosing arms, injections will be administered by study personnel using the investigational device at Week 16.

First treatment for the 1ml device cohort in PS0014 will be the timepoint of first bimekizumab injection in DV0002. First treatment in DV0002 will be the timepoint of first self-injection in DV0002.

After Week 16 in the DV0002 substudy, subjects will continue in PS0014.

2.3.3 Safety Follow-Up

A device Safety Follow-up (SFU) telephone call will occur 1 week after the last self-administration (at DV0002 Week 9).

Subjects who are withdrawn from DV0002 but continue their PS0014 study participation will be required to perform an SFU telephone call 1 week after their final DV0002 dosing visit.

2.3.4 Withdrawal

Subjects who are withdrawn from bimekizumab treatment (PS0014 study) during the course of DV0002 will also be required to follow the PS0014 withdrawal procedures that means subjects will undergo the Premature End of Treatment (PEOT) Visit assessments and will enter the SFU Period.

2.3.5 Study duration per subject

The maximum DV0002 substudy duration will be 16 weeks for each subject. Subjects will then continue to receive treatment in PS0014 for the duration of the PS0014 study.

The end of the DV0002 substudy is defined as the date on which the last subject completes his/her DV0002 Week 16 Visit or withdraws from the study.

2.3.6 Planned number of subjects

For evaluation of the 1mL device, it is planned to enroll approximately 200 subjects; each device arm (bimekizumab-SS-1mL, bimekizumab-AI-1mL) will consist of approximately 100 subjects.

Once the 1mL device cohort has finished enrolling, the 2mL device cohort will start enrolling. For evaluation of the 2mL device, it is planned to enroll approximately 100 subjects; each device arm (bimekizumab SS 2mL or bimekizumab-AI-2mL) will consist of approximately 50 subjects.

It is anticipated that this study will involve up to 80 sites in North America.

2.4 Determination of sample size

This study will not be powered with respect to any endpoint and sample size is based on practical considerations.

1mL Device Cohort

For the 1mL device cohort, to maintain blinding in the PS0014 feeder studies, DV0002 will recruit subjects who were administered bimekizumab 320mg (Q4W or Q8W) and subjects who were administered placebo or ustekinumab in the PS0014 feeder studies. A total of 100 subjects (50 subjects per device arm) are planned for PK trough level analyses, but these analyses can only be performed on subjects who do not change their bimekizumab dose or dosing regimen (ie, 320mg bimekizumab Q4W or Q8W) between the PS0014 feeder studies and the DV0002 substudy. The DV0002 substudy will therefore enroll approximately 200 subjects (to compensate for subjects with bimekizumab dose changes) to ensure that 100 subjects are available for PK trough analysis.

Subjects who enroll in the DV0002 substudy 1mL device cohort will be randomly assigned to the bimekizumab SS 1mL or the bimekizumab AI 1mL device arms (each device arm will consist of approximately 100 subjects). Within each device arm, subjects will be divided into tertiles by BMI; there will be approximately 33 subjects per tertile, which is expected to yield approximately 16 to 17 subjects per tertile who are evaluable for steady state trough PK level analyses.

Subjects are evaluable for steady state trough PK level analyses, if they enter PS0014 on the same drug and dose as completing the feeder study and if they receive the drug at least 16-20 weeks before PS0014. The second condition is automatically fulfilled. Each subject in the feeder study will receive more than 20 weeks of the same treatment in the maintenance phase except escape subjects from PS0013 which are excluded from DV0002 enrollment.

2mL Device Cohort

Once the 1mL device cohort has finished enrolling, the 2mL device cohort will start enrolling. Subjects who participated in the 1mL device cohort of DV0002 are not eligible to enroll in the 2mL device cohort. For evaluation of the 2mL device, it is planned to enroll approximately 100 subjects. Subjects are evaluable for steady state trough PK level analysis if they receive the same bimekizumab administration (frequency and dose) from beginning of PS0014 through to the end of the sub-study. It is expected that most subjects will be evaluable for the PK trough level analyses.

Subjects who enroll in the DV0002 substudy 2mL device cohort will be randomly assigned to the bimekizumab-SS-2mL or the bimekizumab-AI-2mL device arms (each device arm will

consist of approximately 50 subjects). Within each device arm, subjects will be divided into tertiles by BMI; there will be approximately 16 to 17 subjects per tertile who are evaluable for steady state trough PK level analyses.

3 DATA ANALYSIS CONSIDERATIONS

3.1 General presentation of summaries and analyses

Statistical analysis and generation of tables, figures, subject data listings, and statistical output will be performed using SAS Version 9.3 or higher. All tables and listings will use Courier New font size 9.

Descriptive statistics will be displayed to provide an overview of the study results. For continuous variables, descriptive statistics will include number of subjects with available measurements (n), mean, standard deviation (SD), median, minimum, and maximum.

For categorical variables, the number and proportion of subjects, will be presented. In addition, for the primary, secondary and other variables the 90% confidence interval (CI) based on the Exact Binomial, will also be presented. Unless otherwise noted, the denominator for percentages should be based on the number of subjects included in the respective analysis set. Subjects with missing data can generally be accounted for using either of the following approaches:

- For summaries of demographics and Baseline characteristics: summarize percentages based on all subjects in the analysis set and include a "Missing" category (corresponding to subjects with missing data for the variable being summarized) as the last row in the list of categories being summarized.
- For summaries of outcome and safety variables, unless otherwise specified: percentages will be summarized based only on those subjects with observed data for the variable being summarized. As the denominator may be different from the number of subjects in the analysis set being considered, the denominator should be displayed in the table. The general format for displaying this will be "n/NSub (%)."

Percentages will be presented to 1 decimal place. If the percentage is 100 or 0, no decimal will be presented. Typically, the % sign should be presented in the column header, but not with each individual value.

For bimekizumab PK concentrations, summary statistics will include geometric mean, geometric coefficient of variation (CV), 95% confidence intervals for geometric mean, arithmetic mean, SD, median, minimum, and maximum. All summaries of PK variables will be based on the observed values. No imputation will be used.

Decimal places for descriptive statistics will always apply the following rules:

- "n" will be an integer
- Mean, SD, and median will use one additional decimal place compared to the original data
- CV [%] will be presented with one decimal place
- Minimum and maximum will have the same number of decimal places as the original value.

Derived variables in general will display the mean, SD, and median to 1 more decimal place than the variables used in the derivation. If the number of decimal places reported in the raw data is

varied, then use either the maximum raw number of reported decimal places or 3, whichever is the lowest, as a guide for the descriptive statistics.

A complete set of data listings containing all documented data as well as calculated data will be generated

3.2 Analysis Time Points

If the early withdrawal visit occurs at a scheduled visit as outlined in the schedule of assessments, then no mapping is necessary, and any early withdrawal assessments should correspond to that scheduled visit. Premature study withdrawal visit assessments that occur on a date after a scheduled visit will be assigned to the next scheduled site visit per the protocol following the last visit where assessments were available.

3.3 Definition of Baseline values

The Baseline value is defined as the last non-missing measurement prior to the first self-injection at Visit 1 (Baseline).

If a scheduled Baseline assessment is taken on the same day as the first administration of study medication, then the assessment will be assumed to have been performed prior to study medication.

3.4 Relative Day

The relative day will be included in different listings and will be calculated as follows:

- If the start (stop) date occurred on or after the first dose in DV0002, but prior to the drug stop date, relative day is calculated as start (stop) date minus first dose date + 1
- If the start (stop) date occurred after the last dose of bimekizumab, the relative day to the most recent dose is calculated as start (stop) date minus most recent dose date. The relative day in this situation should be preceded by a '+'
- If the start (stop) date occurred before the first dose in DV0002, the relative day is calculated as start (stop) date minus first dose date. The relative day in this situation should be preceded by a '-'.

Relative day will only be computed for fully completed dates and will be missing for partial dates.

3.5 Protocol deviations

Important protocol deviations are deviations from the protocol which could potentially have a meaningful impact on the primary objective of the study. The criteria for identifying important protocol deviations and the classification of important protocol deviations will be defined within the project Data Cleaning Plan.

WHO declared a global COVID-19 pandemic on 11 March 2020. All subjects were recruited into this study during the pandemic and therefore the impact of COVID-19 on the study will be assessed. Deviations related to the Coronavirus Disease 2019 (COVID-19) global pandemic are unavoidable deviations from the protocol due to confirmed COVID-19 infection, suspected COVID-19 infection, general circumstances around COVID-19 without infection or any other deviation from the protocol due to COVID-19. COVID-19 protocol deviations will be reviewed

as part of the ongoing data cleaning process. Any COVID-19 impact protocol deviations that are determined to be important or not-important will be included in this summary. A by-subject listing of COVID-19 related protocol deviations will be provided.

3.6 Analysis sets

3.6.1 1mL Device Cohort

3.6.1.1 Enrolled Set

The Enrolled Set (ES) will consist of all subjects who have given informed consent for DV0002.

3.6.1.2 Safety Set

Two different Safety Sets (SS) will be generated (1 for each device type): the bimekizumab-SS-1mL Safety Set (SS-s) and the bimekizumab-AI-1mL Safety Set (SS-a). Each SS will consist of all subjects in the study who receive at least 1 dose of bimekizumab by the indicated self-injection investigational device. Safety variables will be analyzed using the SS-s and SS-a.

3.6.1.3 Full Analysis Set

Two different Full Analysis Sets (FASs) will be generated (1 for each device type): FAS-s and FAS-a. Each FAS will consist of all subjects in the SS-s or SS-a who self-inject at least 1 dose of bimekizumab using the given device and who have an assessment of self-injection. All self-injection related endpoints will be analyzed using the FAS-s and FAS-a.

3.6.1.4 Pharmacokinetic Per Protocol Set

Two different Pharmacokinetic Per Protocol Sets (PK-PPS) will be generated (1 for each device type): the bimekizumab-SS-1mL PK-PPS (PK-PPS-s) and the bimekizumab-AI-1mL PK-PPS (PK-PPS-a). Each PK-PPS will consist of all subjects who receive the same bimekizumab administration (frequency and dose) in the PS0014 feeder studies as in the DV0002 substudy and who have at least 1 evaluable PK assessment in the DV0002 substudy without important protocol deviations that would affect the concentration. Pharmacokinetic variables will be analyzed using the PK-PPS-s and PK-PPS-a.

All PK assessments after baseline assessments from feeder study will be considered for the requirement of at least one evaluable PK assessment.

3.6.2 2mL Device Cohort

3.6.2.1 Enrolled Set

The Enrolled Set (ES) will consist of all subjects who have given informed consent for DV0002.

3.6.2.2 Safety Set

Two different Safety Sets (SS) will be generated (1 for each device type): the bimekizumab-SS-2mL Safety Set (SS-s) and the bimekizumab-AI-2mL Safety Set (SS-a). Each SS will consist of all subjects in the study who receive at least 1 dose of bimekizumab by the indicated self-injection investigational device. Safety variables will be analyzed using the SS-s and SS-a.

3.6.2.3 Full Analysis Set

Two different Full Analysis Sets (FASs) will be generated (1 for each device type): FAS-s and FAS-a. Each FAS will consist of all subjects in the SS-s or SS-a who self-inject at least 1 dose of

bimekizumab using the given device and who have an assessment of self-injection. All self-injection related endpoints will be analyzed using the FAS-s and FAS-a.

3.6.2.4 Pharmacokinetic Per Protocol Set

Two different Pharmacokinetic Per Protocol Sets (PK-PPS) will be generated (1 for each device type): the bimekizumab-SS-2mL PK-PPS (PK-PPS-s) and the bimekizumab-AI-2mL PK-PPS (PK-PPS-a). Each PK-PPS will consist of all subjects who receive the same bimekizumab administration (frequency and dose) from beginning of PS0014 through to the end of the sub-study and who have at least 1 evaluable PK assessment in the DV0002 substudy without important protocol deviations that would affect the concentration. Pharmacokinetic variables will be analyzed using the PK-PPS-s and PK-PPS-a.

All PK assessments after DV0002 baseline assessments (Week 24, Week 28 or Week 32 from PS0014 study) will be considered for the requirement of at least one evaluable PK assessment.

3.7 Treatment assignment, treatment and device groups

This is an open-label study and as such all subjects will be summarized according to the treatment that was provided. The treatment group will be allocated in PS0014 and the device group will be allocated in DV0002.

PS0014 treatment groups

This refers to the study treatment assigned to the subject at the beginning of PS0014 and does not account for the treatment received in the relevant Feeder Study. The allocation of treatments in PS0014 is done by an algorithm considering the subjects' feeder study (PS0008, PS0009, or PS0013) and PASI90 response at PS0014 study entry. The PS0014 treatment groups are as follows:

- Bimekizumab 320mg Q8W
- Bimekizumab 320mg Q4W.

DV0002 device groups

This refers to the study device assigned to the subject at the beginning of DV0002. The DV0002 1mL device groups are as follows:

- Bimekizumab-SS-1mL
- Bimekizumab-AI-1mL.

The DV0002 2mL device groups are as follows:

- Bimekizumab-SS-2mL
- Bimekizumab-AI-2mL.

The outcome variables will be summarized by PS0014 treatment and DV0002 device group. The different DV0002 device groups are reflected in the use of the corresponding analysis set SS-s, SS-a, FAS-s, FAS-a, PK-PPS-s and PK-PPS-a. For simplification "treatment group" and "device group" will be used in the outputs.

3.8 Center pooling strategy

No pooling of centers is planned for this study.

3.9 Coding dictionaries

All ADEs will be coded and classified by system organ class (SOC), high level term (HLT), and preferred term (PT) according version 19.0 of the Medical Dictionary for Regulatory Activities (MedDRA®).

All medications other than the study drug will be classified by World Health Organization (WHO) Anatomical Therapeutic Chemical (ATC) classification, presenting Anatomical Main Group (ATC Level 1), Pharmacological Subgroup (ATC Level 3), and preferred term (PT), using version SEP/2015 of the World Health Organization Drug Dictionary (WHO-DD), according to UCB standard operating procedures (SOP).

Previous and ongoing medical history will be classified by version 19.0 of MedDRA® SOC and PT.

3.10 Changes to protocol-defined analyses

Subjects who had important protocol deviations affecting the primary outcome variable, as confirmed during ongoing data cleaning meetings prior to database lock, will be not excluded from the FAS-s or FAS-a.

3.10.1 Changes related to COVID-19

COVID-19 protocol deviations have been defined in Section 3.5 and the presentation of COVID-19 protocol deviations is described in Section 5.3.

4 STATISTICAL/ANALYTICAL ISSUES

4.1 Adjustments for covariates

Not applicable.

4.2 Handling of dropouts or missing data

For analyses of ADEs and concomitant medication usage, a complete date must be established in order to correctly identify the ADE or medication as occurring during treatment or not. To calculate the duration of disease, a complete date of onset of plaque psoriasis is needed. For purposes of imputing missing components of partially-reported start and stop dates for ADEs, for medication use, and date of onset of plaque psoriasis, the algorithms listed below will be followed. Start and stop dates of ADEs or concomitant medication will be displayed as reported in the subject data listings (i.e., no imputed values will be displayed in data listings).

Partial ADE and concomitant medication start dates will be imputed as follows:

Imputation of Partial Start Dates

- If only the month and year are specified and the month and year of first dose is not the same as the month and year of the start date, then use the 1st of the month
- If only the month and year are specified and the month and year of first dose is the same as the month and year of the start date, then use the date of first dose

- If only the year is specified, and the year of first dose is not the same as the year of the start date, then use the 1st of January of the year of the start date
- If only the year is specified, and the year of first dose is the same as the year of the start date, then use the date of first dose
- If the start date is completely unknown and the stop date is unknown or not prior to the date of first dose, then use the date of first dose.

Imputation of Partial Stop Dates

- If only the month and year are specified, then use the last day of the month
- If only the year is specified, then use December 31st of that year
- If the stop date is completely unknown, do not impute the stop date.

If the (imputed) stop date is prior to the imputed start date:

- If only the month and year are specified and the month and year of first dose is the same as the month and year of the start date and the stop date is before the date of first dose, then set the start date to the 1st of that month.
- If only the year is specified, and the year of first dose is the same as the year of the start date, and the stop date is before the date of first dose, then use the 1st of January of the year of the start date

Partial start dates for onset date of plaque psoriasis will be imputed as follows:

- If only the month and year are specified, then use the last day of the month.
- If only the year is specified, then use the 31st of December of the year.
- If the start date is completely unknown, do not impute the start date.

In the event of ambiguity or incomplete data which makes it impossible to determine whether a medication was concomitant or an adverse event was treatment emergent, the medication will be considered as concomitant or the adverse event will be considered treatment emergent.

If the intensity of an ADE is unknown, it will be considered as severe.

There will be no special procedures for handling missing data for any other data points.

4.3 Interim analyses and data monitoring

No interim analysis is planned for this study. No Data Monitoring Committee will be established for this study.

The subjects of DV0002 are ongoing subjects of PS0014. Data cut off for the 1mL final analysis will be last subject last Week 16 visit in DV0002 in the 1mL device cohort. Data cut off for the 2mL final analysis will be last subject last Week 16 visit in DV0002 in the 2mL device cohort. Data cut off rules will be applied for ongoing adverse device events and ongoing concomitant medication.

4.4 Multicenter studies

Individual center results will not be directly presented. Centers are only located in North America (United States and Canada).

4.5 Multiple comparisons/multiplicity

Not applicable.

4.6 Use of an efficacy subset of subjects

Not applicable.

4.7 Active-control studies intended to show equivalence

Not applicable.

4.8 Examination of subgroups

Not applicable.

5 STUDY POPULATION CHARACTERISTICS

5.1 Subject disposition

All subject disposition tables will use the PS0014 treatment groups BKZ 320mg Q8W and BKZ 320mg Q4W and an overall treatment group category (BKZ Total).

The disposition of subjects including the number of subjects in ES and all device-specific analysis sets (SS-s, FAS-s, PKS-s or SS-a, FAS-a, PKS-a) will be summarized. This summary will be based on ES and will present subjects overall and by site in North America.

The disposition of ES will present all bimekizumab treated subjects by PS0014 treatment group and broken out by DV0002 device group.

The number and percentage of subjects who entered the substudy, completed, discontinued with the reasons for discontinuation of the substudy will be presented. This summary will be based on the ES and will present all bimekizumab treated subjects by PS0014 treatment group and broken out by DV0002 device group.

Subjects will be counted as completer if they completed the DV0002 Week 16 visit.

The following listings for subject disposition will be produced based on the ES and presented by PS0014 treatment group/ DV0002 device group:

- A listing of subjects who did not meet study eligibility criteria
- A listing of subject disposition
- A listing of study discontinuation
- A listing of visit dates
- A listing of subjects excluded from analysis sets.
- A listing of subject analysis sets

5.2 Protocol deviations

A summary of number and percentage of subjects with an important protocol deviation (including a summary of subjects excluded from any analysis set due to important protocol deviations) by treatment group will be provided for the SS-a and SS-s.

A by-subject listing of important protocol deviations will be provided.

5.3 COVID-19 Impact

For study participants impacted by the COVID-19 global pandemic, data were collected on a separate eCRF. This form was collected for study visits that were affected by COVID-19, and it collected how the visits were impacted by the pandemic (e.g., performed out of window, done by telephone instead of on-site, not done, etc).

Based on how the visit was affected by the global pandemic, all visits will have a variable indicating how the visit was performed:

- Visit not done at all
- Visit done by video call
- Visit done by telephone
- Visit done at different time point than planned / out of window

Additionally, for visits that are affected by COVID-19, all assessments that are missing will be flagged as missing due to COVID-19. Further, the specific reason of missing data will be captured as the following flags:

- Confirmed COVID-19 infection
- Suspected COVID-19 infection
- General circumstances around COVID-19 without infection
- Other

A summary of number and percentage of subjects with COVID-19 related protocol deviations and COVID-19 related device protocol deviations by treatment group and visit will be provided for the SS-a and SS-s. This summary on COVID-19 related protocol deviations will also be repeated by country.

A by-site, subject and visit listing of COVID-19 related protocol deviations along with a listing of COVID-19 related device protocol deviations will be provided.

6 DEMOGRAPHICS AND OTHER BASELINE CHARACTERISTICS

All summaries detailed in this section will be performed on the SS-a and SS-s and by PS0014 treatment group.

6.1 Demographics

Demographic variables will be summarized by PS0014 treatment group and all bimekizumab treated subjects.

The following continuous variables will be summarized using descriptive statistics (number of subjects, mean, SD, minimum, median and maximum).

- Age at the time of feeder study entry (years)
- Height (cm)
- DV0002 Baseline Weight (kg): will be derived from the weight from the last visit of the feeder study for 1mL device cohort and 2mL cohort subjects.
- DV0002 Baseline BMI (kg/m2)
- BMI (kg/m2) will be calculated as:

$$BMI = \frac{\text{Weight (kg)}}{(\text{Height (m)})^2}$$

The following categorical variables will be summarized using frequency counts and percentages.

- Age group (≤18, 19-<65, ≥65 years)
- DV0002 Baseline Body Weight (≤100kg, >100kg)
- BMI (<25 kg/m2, 25 to <30 kg/m2, ≥30 kg/m2)
- BMI tertiles (≤t1 kg/m2, >t1 kg/m2 to ≤ t2 kg/m2, >t2 kg/m2) based on the respective PK-PPS populations (PK-PPS-s, PK-PPS-c)
- Gender
- Race
- Ethnicity
- Country

By-subject listings of demographics will be provided.

6.2 Other Baseline characteristics

Baseline characteristics will be summarized by treatment group and overall.

Generally, the following continuous variables will be summarized using descriptive statistics (number of subjects, mean, SD, minimum, median and maximum).

- Duration of disease (years)

Duration of disease (years) will be calculated as:

$$\text{Disease Duration} = \frac{(\text{Date of randomization in DV0002} - \text{Date of onset of Plaque Psoriasis}^1)}{365.25}$$

[1]If the date of onset of plaque psoriasis is partial, it should be imputed to the most recent feasible date (ie, last day of the month if only day is missing, or the last day of the year if day and month

are missing). Note that if the date of randomization is missing then the duration of disease will be derived using the date of screening.

The following categorical variables will be summarized using frequency counts and percentages.

- Duration of disease (<median, ≥median).

6.3 Medical history and concomitant diseases

Previous and ongoing medical history collected at the start of the feeder study will be based on SS-s and SS-a and summarized by treatment groups, system organ class (SOC) and preferred term (PT) using MedDRA®. Medical history and psoriasis history will be included in the summary tables and listings for medical history. Medical procedures are not coded.

Previous and ongoing medical history along with the updated medical history collected at the end of the feeder studies will be presented in a by-subject listing for SS-s and SS-a, respectively.

6.4 Prior and concomitant medications

Concomitant medication details are collected at each visit of DV0002. Concomitant medications are medications taken at least one day in common with the DV0002 study medication dosing period (DV0002 Baseline to DV0002 Week 16).

All concomitant medication will be listed for SS-s and SS-a, respectively.

Concomitant medication which started before DV0002 Week 16 and were ongoing at the data cut off will be included with the status remaining as ongoing. Concomitant medication which were ongoing at DV0002 Week 16 but with an end date before the data cut off will be included with their end date as recorded.

For 2 ml phase analysis, concomitant medications include those started on or before the later of the final contact date or (the last injection date + 7 days).

7 MEASUREMENTS OF TREATMENT COMPLIANCE

During the Treatment Period of this study, IMP administration (either self-administration or study personnel-administration) will be performed in the clinic and observed by the Investigator or his/her designee; monitoring subject compliance is therefore not applicable.

8 EFFICACY ANALYSES

No efficacy summaries are planned for the DV0002 substudy.

9 PHARMACOKINETICS AND PHARMACODYNAMICS

9.1 Pharmacokinetics

The statistical analyses of the PK data will be descriptive in nature and will be summarized using the relevant device-specific population (PK-PPS-s or PK-PPS-a). Data will be analyzed overall for each device by injection type (self-administered or study personnel-administered), by injection site (abdomen or thigh), and by BMI category. The BMI categories will be defined into three tertiles within each device arm PK-PPS analysis set and device cohort and derived from subjects' DV0002 Baseline BMI values.

To allow for an analysis of PK trough levels for bimekizumab administration via self-injection or via study personnel administration, pre-dose PK samples will be taken throughout the DV0002

substudy. For the Q4W dose regimen, PK trough levels will be determined based on pre-dose PK sampling at DV0002 Baseline and DV0002 Week 8 for the study personnel administration and at DV0002 Week 4 and DV0002 Week 12 for the self-administration trough levels, respectively. For the Q8W dose regimen, PK trough levels will be determined based on pre-dose PK sampling at DV0002 Baseline for the study personnel administration and at DV0002 Week 8 and DV0002 Week 16 for the self-administration trough levels, respectively. For the 1ml device cohort, DV0002 Baseline PK samples are the PK samples from the last visit of the feeder studies.

For the analysis of PK trough levels by injection site (abdomen or thigh) and by BMI category (by tertiles), self-administration PK trough levels and study personnel administration PK trough levels will be used.

PK samples for self-administration where the injection was done by site personnel or caregiver will be listed but not be used for summary statistics. PK samples for personnel administration where the injection was done by the subject will be listed but not be used for summary statistics.

Only pre-dose (trough) concentrations will be included while summarizing tables and figures. If the dosing for a visit is +/- 7 days out of window then the plasma concentration from that visit and all subsequent visits will be excluded from the PK summary. PK samples collected after dosing will be excluded from summary statistics.

PK summaries will be based on observed values. No imputation will be used. However, if plasma concentration measurements are below the level of quantification, then for calculation of the derived statistics the result will be set to ½ of the lower level of quantification (LLOQ). Descriptive statistics including geometric mean, geometric coefficient of variation, and geometric mean 95% CI if applicable will be calculated if at least 2/3 of the values of interest are above the LLOQ. If this is not the case, only median, minimum, and maximum will be presented.

Boxplots of plasma concentration will be presented by visit and by treatment group.

All PK results will be listed.

In addition, the PK results from all subjects not in PK-PPS-s or PK-PPS-a will be listed based on the SS-a and SS-s.

9.2 Pharmacodynamics

Not applicable.

10 SAFETY ANALYSES

All safety analysis will be performed for SS-a and SS-s and by treatment group.

10.1 Extent of exposure

Extent of exposure is not relevant for the DV0002 substudy. Occurrence of Adverse device effects in this substudy will not be affected by the duration of medication exposure.

10.2 Adverse events

All AEs (including serious adverse events [SAEs]) will be reported in a common database for PS0014 and DV0002, but only adverse device effects (ADEs), serious adverse device effects (SADEs), and device deficiencies will be summarized in the DV0002 substudy. Specifically, only those AEs related to the use of the investigational medical devices bimekizumab-SS-

1mL,bimekizumab-AI-1mL, bimekizumab-SS-2 mL or bimekizumab-AI-2 mL (based on the Investigator's judgement) will be assessed. All AEs (including SAEs) which are not assessed to be related to the investigational devices will be summarized separately in the report for the main study PS0014. An exception are AEs that are indicated as injection site reactions during self-injection. These will be listed in DV0002 as well as in PS0014.

10.2.1 Adverse device effects

Adverse events are recorded at the AE CRF page at the time when they occur. If an adverse event is related to the device by assessment of the investigator it is counted as an Adverse device event. For DV0002 only ADE will be considered which started during the DV0002 study period. And ADEs started in the 1 ml phase will be included for 1 ml phase analysis, and those started in the 2 ml phase will be included for the 2 ml phase analysis. For 2 ml phase analysis, adverse device effects include those that started on or before the later of the final contact date or (the last injection date + 7 days).

All ADE data will be listed and no statistical testing will be performed. Only treatment-emergent ADEs will be included in the summary tables. Treatment-emergent ADEs (TEADEs) will be defined as events that have a start date on or following the first self-administration of study treatment in DV0002 through the final self-administration of study treatment + 7 days. The device SFU will occur 1 week after the last self-administration.

All ADEs will be coded and classified by system organ class, high level term, and preferred term. Adverse device effects will be summarized by the frequency and percentage of subjects having 1 or more of the events in question. Additional planned summaries include overall ADEs and SADEs. All summaries are presented by PS0014 treatment

- Incidence of TEADEs – Overview
- Incidence of TEADEs by SOC, HLT, and PT
- Incidence of serious TEADEs by SOC, HLT, and PT
- Incidence of TEADEs leading to death
- Incidence of TEADEs leading to discontinuation
- Incidence of non-TEADEs (only listed and not summarized in a table)

For definition of serious, unanticipated and serious unanticipated ADEs see protocol of DV0002.

Adverse device effects which started before DV0002 Week 16 and were ongoing at the data cut off will be included with the status remaining as ongoing. Adverse device effects which were ongoing at DV0002 Week 16 but with an end date before the data cut off will be included with their end date as recorded.

10.2.2 Injection site reaction

Injection site reactions are recorded at the AE CRF page at the time when they occur. All AEs will be coded and classified by system organ class, high level term, and preferred term. An AE with High Level Terms of "Administration site reactions NEC" and "Injection site reactions" will be evaluated as injection site reaction.

All injection site reactions for self-injection with a start date on or following the first self-administration of study treatment through the final self-administration of study treatment + 7 days will be listed.

10.3 Clinical laboratory evaluations

All clinical laboratory evaluations including hematology, chemistry and urinalysis will be collected in PS0014.

10.4 Vital signs, physical findings, and other observations related to safety

eCRF data of vital signs, Electrocardiograms, physical examination and pregnancy test results will be collected in PS0014.

11 OTHER ANALYSES

This section contains a detailed description of the analysis of the primary, secondary and other outcome variables. All statistical analyses will be descriptive in nature. No inferential statistical analyses are planned. The analysis is done on FAS-s and FAS-a, respectively.

11.1 Primary outcome

The primary outcome variable is the percentage of all subjects able to self-administer safe and effective injections using the given device at DV0002 Week 8. Safe and effective self-injection will be
evaluated by the study personnel as defined below:

- Complete dose delivery: Subject self-injects the complete dose of bimekizumab as confirmed by a visual inspection of the investigational device which shows that the IMP is delivered completely (ie, container is empty), and
- No ADEs that would preclude continued use of the device for self-injection (ie, no SADEs and/or ADEs leading to withdrawal from the DV0002 substudy).

All data to assess the primary outcome is collected on the subject self-injection of bimekizumab CRF page for DV0002 Week 8. For the number of subjects with safe and effective self-injections simply the cases which indicated “yes” for the question “Did the subject self-inject the complete dose of Bimekizumab” and “no” for the question “Where there any AEs related to use of the investigational device for self-injection” at Week 8 are counted.

For subjects in the 1mL device cohort, two self-injections will be performed at DV0002 Week 8 and the questions will be answered twice. If the answers are different between both self-injections in one visit, then the worst case of both answers will be used for analysis at this visit. Subjects with only one self-injection at one visit will be counted as non-responder. Assessments where the self-injection was not performed by the subject will be not included in any summary statistics.

The number and percentage of subjects with safe and effective self-injections will be tabulated separately for each device overall and within each device by dosing regimen. The 90% CIs based on the Exact Binomial method will be reported as well.

11.2 Secondary outcome

The secondary outcome variable is the percentage of subjects able to self-administer safe and effective injections using the given device at DV0002 Baseline (first self-injection visit). Safe and effective self-injection will be evaluated by the study personnel. The secondary outcome variables will be analyzed in the same manner as the primary outcome variable.

All data to assess the secondary outcome is collected on Subject self-injection of Bimekizumab CRF page for DV0002 Baseline.

11.3 Other outcomes

The other outcome variables will be summarized using descriptive statistics and they will be tabulated separately for each device overall based and within each device by PS0014 treatment.

Assessments where the self-injection was not performed by the subject will be not included in any summary statistics.

11.3.1 Pre-injection SIAQ (versions 2.0 and 2.1)

The pre-injection SIAQ (versions 2.0 and 2.1) will be completed at DV0002 Baseline. Version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL and bimekizumab-SS-2mL and version 2.1 of the SIAQ will be used to assess bimekizumab-AI-1mL and bimekizumab-AI-2mL. There are no differences in Version 2.0 to Version 2.1 in pre-injection SIAQ.

The pre-injection SIAQ consists of 7 items each with a scale of 1 to 5. There are three individual subscales (feelings about injections [FL, 3 items], self-confidence [CO, 3 items] and satisfaction with current mode of administration [SA, 1 item]). Each subscale score will be calculated using the average of the individual transformed item scores. The item score will be transformed using the following rule:

$$Transformed\ Item\ Score = \big((raw\ item\ score) - 1\big) \times 2.5$$

In the case of missing values, no domain score will be calculated if more than 50% of the items within the domain are missing.

Higher individual scores of the pre-injection SIAQ indicate more confidence, higher satisfaction and less concerns with self-injections.

Summary statistics for all individual items and each subscale will be produced for Baseline.

11.3.2 Post-injection SIAQ (versions 2.0 and 2.1)

The post-injection SIAQ (versions 2.0 and 2.1) will be completed at DV0002 Baseline and DV0002 Week 8. Version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL and bimekizumab-SS-2mL and version 2.1 of the SIAQ will be used to assess bimekizumab-AI-1mL and bimekizumab-AI-2mL. Version 2.0 and version 2.1 of the SIAQ are identical, except for Question 11 due to different handling of the devices.

The post-injection SIAQ consists of 21 items on 6 individual subscales (FL [3 items], self-image [IM, 1 item], CO [3 items], Injection-site reactions [RE, 2 items], ease of use [EU, 5 items) and satisfaction with self-injection [SA, 7 items]). The items of the individual subscale EU have a score range of 1 to 6, the other individual subscales have a score range of 1 to 5. Each subscale score will be calculated using the average of the individual transformed item scores. The item scores for the EU subscale will be transformed using the following rule:

$$Transformed\ Item\ Score = \big((raw\ item\ score) - 1\big) \times 2$$

The item scores for the other subscales will be transformed using the following rule:

$$Transformed\ Item\ Score = \big((raw\ item\ score) - 1\big) \times 2.5$$

In the case of missing values, no domain score will be calculated if more than 50% of the items within the domain are missing.

Higher individual scores of the post-injection SIAQ indicate more confidence, higher satisfaction and less concerns with self-injections.

Summary statistics for all individual items and each subscale will be produced for DV0002 Baseline and DV0002 Week 8.

11.3.3 Injection site pain

The visual analog scale of injection site pain indicates the level of pain during the injection. It ranges from 0-100 mm with higher values indicating more severe pain and 0 for no pain.

Summary statistics of actual values and change from DV0002 Baseline values will be used to summarize injection site pain by visit after self-injection.

11.3.4 Structural and mechanical integrity of the devices

The structural and mechanical integrity of the device after completion of self-injection will be assessed by the investigate after each injection in the 'subject self-injection of bimekizumab" CRF page. The assessment will be done using the questions for structural integrity and function compromise. The structural integrity is based on a visual examination of the device that shows clear evidence of damage, compromised structural integrity not superficial and/or cosmetic imperfections. The functional compromise will be based on a visual examination of the device that shows clear evidence of damage and/or device dose not function normally. Both questions will be separately summarized.

Two injections will be performed at each self-injection visit. At each injection the device could be replaced. Percentages will be based on the total number of devices used.

Frequency tables will be produced to show the number and percentage of devices with:

- used bimekizumab-SS-1mL, bimekizumab-AI-1mL, bimekizumab-SS-2mL and bimekizumab-AI-2mL syringes identified as having structural integrity issues after completion of self-injection.
- used bimekizumab-SS-1mL, bimekizumab-AI-1mL, bimekizumab-SS-2mL and bimekizumab-AI-2mL syringes identified as functionally compromised.

The 90% CIs based on the Exact Binomial method will be reported as well.

12 REFERENCES

Coteur G (2005) SIAQ©v2 User Manual (2nd Ed). UCB, Braine L'Alleud, Belgium.

13 APPENDICES

13.1 SAP Amendment 1

Rationale for the amendment

This protocol has been amended to add the evaluation of the 2mL self-injection devices developed by UCB: a 2mL bimekizumab safety syringe (bimekizumab-SS-2mL) and a 2mL bimekizumab auto-injector (bimekizumab-AI-2mL).

Modifications and changes

Global changes:

The following changes were made throughout the SAP:

- The DV0002 study number was added before the study visit where it was necessary to distinguish it from the PS0014 study visits.
- The list of abbreviations was updated accordingly.
- Minor spelling, editorial, and formatting changes were made throughout the document.

Specific changes

In addition to the global changes, the following specific changes have been made (formats as missing spaces or redundant spaces are not listed, typos):

Change #1

The following abbreviation has been added:

bimekizumab-AI-2mL	2mL bimekizumab auto-injector
bimekizumab-SS-2mL	2mL bimekizumab safety syringe

The following abbreviation has been updated:

FAS-a	Full Analysis Set for the bimekizumab-AI-1mL **Full Analysis Set for the bimekizumab-AI-2mL**
FAS-s	Full Analysis Set for the bimekizumab-SS-1mL **Full Analysis Set for the bimekizumab-SS-2mL**
PK-PPS-a	Pharmacokinetic Per Protocol Set for the bimekizumab-AI-1mL **Pharmacokinetic Per Protocol Set for the bimekizumab-AI-2mL**
PK-PPS-s	Pharmacokinetic Per Protocol Set for the bimekizumab-SS-1mL **Pharmacokinetic Per Protocol Set for the bimekizumab-SS-2mL**
SS-a	Safety Set for the bimekizumab-AI-1mL **Safety Set for the bimekizumab AI 2mL**

SS-s	Safety Set for the bimekizumab-SS-1mL **Safety Set for the bimekizumab SS 2mL**

Change #2

Section 1 Introduction

The SAP is based on the following study document: Protocol DV0002, 26 Jul 2018. All references to study protocol hereafter refer to this version of the protocol.

Has been changed to:

The SAP is based on the following study document:

- **Final** Protocol DV0002, 26 Jul 2018.
- **Protocol amendment 1, 28 Oct 2019.**

All references to study protocol hereafter refer to this version of the protocol.

All analyses will be performed separately for the 1mL device cohort and for the 2mL device cohort. Once subjects in the 1mL device cohort complete DV0002, a final analysis will be performed for that cohort, and a clinical study report will be prepared. A separate final analysis will be performed for the 2mL device cohort once all data have been collected and will be reported separately from the initial clinical study report.

Change #3

Section 2.1.1 Primary objective

The primary objective of the study is to evaluate for each device the ability of subjects with moderate to severe chronic plaque PSO to safely and effectively self-inject bimekizumab 8 weeks after training in the self-injection technique using the bimekizumab-SS-1mL or the bimekizumab-AI-1mL.

Has been changed to:

The primary objective of the study is to evaluate**,** for each device**,** the ability of subjects with moderate to severe chronic plaque PSO to safely and effectively self-inject bimekizumab 8 weeks after training in the self-injection technique ~~using the bimekizumab-SS-1mL or the bimekizumab-AI-1mL~~.

Change #4

Section 2.1.2 Secondary objective

The secondary objective of the study is to evaluate the ability of subjects with moderate to severe chronic plaque PSO to safely and effectively self-inject bimekizumab immediately after training in self-injection technique using the bimekizumab-SS-1mL or the bimekizumab-AI-1mL.

Has been changed to:

The secondary objective of the study is to evaluate**, for each device,** the ability of subjects with moderate to severe chronic plaque PSO to safely and effectively self-inject bimekizumab immediately after training in self-injection technique using the ~~bimekizumab-SS-1mL or the bimekizumab-AI-1mL~~ **devices**.

Change #5

Section 2.1.3 Other objectives

Other objectives of the study are to evaluate the following:

- Subject experience of self-injection as assessed by the pain visual analog scale (VAS) and the Self-injection Assessment Questionnaire (SIAQ).
- Trough PK (trough bimekizumab) levels associated with self-injection using the test device, injection by study personnel using the 1mL PFS, injection site (abdomen or thigh), and BMI category (by tertile).
- The structural and mechanical integrity of the bimekizumab-SS-1mL and the bimekizumab-AI-1mL after completion of self-injection.
- The overall safety and tolerability of self-injections.

Has been changed to:

Other objectives of the study are to evaluate the following:

- Subject experience of self-injection **using the investigational devices** as assessed by the pain visual analog scale (VAS) and the Self injection Assessment Questionnaire (SIAQ).
- Trough PK (trough bimekizumab) levels associated with self-injection using the ~~test device~~ **investigational devices**, injection by study personnel ~~using the 1mL PFS~~, injection site (abdomen or thigh), and BMI category (by tertile).
- The structural and mechanical integrity of the ~~bimekizumab-SS-1mL and the bimekizumab-AI-1mL~~**investigational devices** after completion of self-injection.
- The overall safety and tolerability of self-injections **using the investigational devices**.

Change #6

Section 2.2.1 Primary outcome variable

The primary outcome variable is the percentage of subjects able to self-administer safe and effective injections using the bimekizumab-SS-1mL or the bimekizumab-AI-1mL, respectively, at Week 8. Safe and effective self-injection will be evaluated by the study personnel and is defined as:

- Complete dose delivery: Subject self-injects the complete dose of bimekizumab as confirmed by a visual inspection of the bimekizumab-SS-1mL or the bimekizumab-AI-1mL which shows that the IMP is delivered completely (ie, container is empty), and
- No ADEs that would preclude continued use of the device for self-injection (ie, no SADEs and/or ADEs leading to withdrawal from the DV0002 substudy).

In the DV0002 substudy, the 320mg bimekizumab dose will be administered as two 160mg injections with either 2 bimekizumab-SS-1mL devices or 2 bimekizumab-AI-1mL devices. Each self-injection will be evaluated for safety and effectiveness by study personnel using the above criteria. The endpoint of safe and effective self-injection will be met only if both self-injections are determined to be safe and effective.

Has been changed to:

The primary outcome variable is the percentage of subjects able to self-administer safe and effective injections using the bimekizumab-SS-1mL ~~or the,~~ bimekizumab-AI-1mL, ~~respectively, at Week~~ **bimekizumab-SS-2mL, or bimekizumab-AI-2mL**, 8 **weeks after training in self-injection technique**. Safe and effective self-injection will be evaluated by the study personnel and is defined as:

- Complete dose delivery: Subject self-injects the complete dose of bimekizumab as confirmed by a visual inspection of the ~~bimekizumab-SS-1mL or the bimekizumab-AI-1mL~~ device which shows that the IMP is delivered completely (ie, container is empty), and
- No ADEs that would preclude continued use of the device for self-injection (ie, no SADEs and/or ADEs leading to withdrawal from the DV0002 substudy).

In the DV0002 substudy, **for the 1mL devices**, the 320mg bimekizumab dose will be administered as two 160mg injections with either 2 bimekizumab-SS-1mL devices or 2 bimekizumab-AI-1mL devices. Each self-injection will be evaluated for safety and effectiveness by study personnel using the above criteria. The endpoint of safe and effective self-injection will be met only if both self-injections are determined to be safe and effective.

For the 2ml devices, the 320mg bimekizumab dose will be administered as 1 injection with either 1 bimekizumab-SS-2mL or 1 bimekizumab-AI-2mL device. Each self-injection will be evaluated for safety and effectiveness by study personnel using the above criteria. The endpoint of safe and effective self-injection will be met if the single self-injection is determined to be safe and effective.

Change #7

Section 2.2.2 Secondary outcome variable

The secondary outcome variable is the percentage of subjects able to self-administer safe and effective injections using the bimekizumab-SS-1mL or the bimekizumab-AI-1mL at Baseline (the first self-injection visit, immediately after training in self-injection technique). Safe and effective self-injection will be evaluated by study personnel and is defined as for the primary outcome variable (see Section 2.2.1).

Has been changed to:

The secondary outcome variable is the percentage of subjects able to self-administer safe and effective injections using the bimekizumab-SS-1mL**,** ~~or the~~ bimekizumab-AI-1mL**, bimekizumab-SS-2mL, or 1 bimekizumab-AI-2mL** at **DV0002** Baseline (the first self-injection visit, immediately after training in self-injection technique). Safe and effective self-injection will be evaluated by study personnel and is defined as for the primary outcome variable (see Section 2.2.1).

Change #8

Section 2.2.3.1 Outcome variables

The other outcome variables are:

- Responses to pre-injection SIAQ (versions 2.0 and 2.1) at Baseline.

Whenever SIAQ is assessed, version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL and version 2.1 of the SIAQ will be used to assess bimekizumab-AI-1mL (see Section 11.3.1 and Section 11.3.2).

- Responses to post-injection SIAQ (versions 2.0 and 2.1) by visit following self-injection using the assigned device at Baseline and Week 8.
- Injection site pain (using a VAS; 100mm) by visit after self-injection at Baseline and Week 8.
- Percentage of used bimekizumab-SS-1mL and bimekizumab-AI-1mL identified as having structural or mechanical integrity issues after completion of self-injection. This is based on a visual examination of the device that shows clear evidence of damage and/or compromised structural or mechanical integrity.

Has been changed to:

The other outcome variables are:

- Responses to pre-injection SIAQ (versions 2.0 and 2.1) at **DV0002** Baseline.

  Whenever SIAQ is assessed, version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL and **bimekizumab-SS-2mL and** version 2.1 of the SIAQ will be used to assess bimekizumab-AI-1mL **and bimekizumab-AI-2mL** (see Section 11.3.1 and Section 11.3.2).
- Responses to post-injection SIAQ (versions 2.0 and 2.1) by visit following self-injection using the assigned device at **DV0002** Baseline and Week 8.
- Injection site pain (using a VAS; 100mm) by visit after self-injection ~~at~~ **using the assigned device at DV0002** Baseline and Week 8.
- Percentage of used ~~bimekizumab-SS-1mL and bimekizumab-AI-1mL~~ **devices** identified as having structural or mechanical integrity issues after completion of self-injection. This is based on a visual examination of the device that shows clear evidence of damage and/or compromised structural or mechanical integrity.

Change #9

Section 2.2.3.2 Pharmacokinetic variable

The PK variable is trough PK (bimekizumab) levels associated with self-injection using the test device, injection by study personnel using the 1mL PFS, injection site (abdomen or thigh), and BMI category (by tertile). Trough levels will be assessed at Baseline, Week 4, Week 8, and Week 12 for subjects who receive bimekizumab Q4W and trough levels will be assessed at Baseline, Week 8, and Week 16 for subjects who receive bimekizumab Q8W.

Has been changed to:

The PK variable is trough PK (bimekizumab) levels associated with self-injection using the ~~test~~ **investigational** device, injection by study personnel ~~using the 1mL PFS~~, injection site (abdomen or thigh), and BMI category (by tertile). Trough levels will be assessed at **DV0002** Baseline, Week 4, Week 8, and Week 12 for subjects who receive bimekizumab Q4W and trough levels

will be assessed at **DV0002** Baseline, Week 8, and Week 16 for subjects who receive bimekizumab Q8W.

Change #10

Section 2.3.1 Study description

DV0002 is a Phase 3 open-label, randomized, noncomparator, North America-only substudy to PS0014. PS0014 will evaluate the long-term safety, tolerability, and efficacy of bimekizumab in subjects with moderate to severe chronic plaque PSO; study personnel will administer bimekizumab to subjects in a 1mL PFS. The DV0002 substudy will evaluate 2 self-injection investigational devices: the 1mL bimekizumab-SS-1mL and the 1mL bimekizumab-AI-1mL.

In the DV0002 substudy, the safe and effective use of the bimekizumab-SS-1mL or the bimekizumab-AI-1mL for the sc self-injection of bimekizumab by subjects with PSO will be evaluated.

Subjects from selected sites in the PS0014 feeder studies PS0008, PS0009, and PS0013 will be eligible for the DV0002 substudy. The DV0002 substudy will maintain all study assessments of the main PS0014 study from Baseline to Week 16 (inclusive). However, only subjects in the DV0002 substudy will self-administer bimekizumab. At DV0002 Baseline, each subject will be provided with training in self-injection and will receive the IFU and any other applicable training materials. Subjects in the DV0002 substudy will perform self-injections at Baseline (corresponding to the Baseline Visit of PS0014) with a subsequent self-injection at Week 8 (corresponding to Week 8 of PS0014).

Has been changed to:

DV0002 is a Phase 3 open-label, randomized, noncomparator, North America-only substudy to PS0014. PS0014 will evaluate the long-term safety, tolerability, and efficacy of bimekizumab in subjects with moderate to severe chronic plaque PSO; study personnel will administer bimekizumab to subjects in a 1mL PFS. ~~The DV0002 substudy will evaluate 2 self-injection investigational devices: the 1mL bimekizumab-SS-1mL and the 1mL bimekizumab-AI-1mL.~~

In the DV0002 substudy, the safe and effective use of the bimekizumab-SS-1mL ~~or the~~, bimekizumab-AI-1mL, **bimekizumab-SS-2mL, or the bimekizumab-AI-2mL** for the sc self-injection of bimekizumab by subjects with PSO will be evaluated.

Subjects from selected sites in the PS0014 feeder studies PS0008, PS0009, and PS0013 will be eligible for the DV0002 substudy. ~~The DV0002 substudy will maintain all study assessments of the main PS0014 study from Baseline to Week 16 (inclusive). However, only subjects in the DV0002 substudy will self-administer bimekizumab.~~ At DV0002 Baseline, each subject will be provided with training in self-injection and will receive the IFU and any other applicable training materials.

For the 1mL device cohort, subjects~~Subjects~~ in the DV0002 substudy will perform self-injections at DV0002 Baseline (corresponding to the Baseline Visit of PS0014) with a subsequent self-injection at DV0002 Week 8 (corresponding to Week 8 of PS0014).

To allow flexible enrollment, subjects may be randomized in the 2mL device cohort at the PS0014 Week 24, Week 28, or Week 32 visit for subjects receiving bimekizumab Q4W or the PS0014 Week 24 or Week 32 visit for subjects receiving bimekizumab Q8W.

For the 2mL device cohort, subjects will perform self-injections at DV0002 Baseline with a subsequent self-injection 8 weeks after training. The 2mL device cohort will evaluate 2 self-injection devices: the bimekizumab SS 2mL and the bimekizumab AI 2mL.

Change #11

Section 2.3.2 Treatment Period

During the 16-week Treatment Period of DV0002, subjects will receive either bimekizumab 320mg Q8W or bimekizumab 320mg Q4W, based on their assigned dose at Baseline. Baseline for DV0002 and Baseline for PS0014 will occur at the same time.

Eligible subjects will be randomly assigned in a 1:1 ratio to perform self-injection using either the bimekizumab-SS-1mL or the bimekizumab-AI-1mL. Regardless of the assigned dose regimen, subjects will perform self-injection with the assigned device only at Baseline (corresponding to the Baseline Visit of PS0014) and at Week 8 (corresponding to Week 8 of PS0014). For subjects in the bimekizumab 320mg Q4W dosing arm, injections will be administered by study personnel using the 1mL PFS at Week 4 and Week 12; for subjects in both dosing arms, injections will be administered by study personnel using the 1mL PFS at Week 16. After Week 16 in the DV0002 substudy, subjects will continue in PS0014 (the next visit after DV0002 completion will be the Week 20 Visit in PS0014).

Has been changed to:

During the 16-week Treatment Period of DV0002, subjects will receive either bimekizumab 320mg Q8W or bimekizumab 320mg Q4W, based on their assigned dose at **PS0014** Baseline. Baseline for DV0002 and Baseline for PS0014 will occur at the same **time for the 1mL device cohort. In the 2mL device cohort, Baseline for DV0002 will occur at the PS0014 Week 24, Week 28, or Week 32 visit for subjects receiving bimekizumab Q4W or the PS0014 Week 24 or Week 32 visit for subjects receiving bimekizumab Q8W**.

Eligible subjects **(PS0014 entry criteria and DV0002 entry criteria)** will be randomly assigned in a 1:1 ratio to perform self-injection using either the bimekizumab-SS-1mL or the bimekizumab-AI-1mL **for the 1mL device cohort or using either the bimekizumab-SS-2mL or the bimekizumab-AI-2mL for the 2mL device cohort**. Regardless of the assigned dose regimen, subjects will perform self-injection with the assigned device only at **DV0002** Baseline ~~(corresponding to the Baseline Visit of PS0014)~~ and at **DV0002** Week 8 ~~(corresponding to Week 8 of PS0014)~~. For subjects in the bimekizumab 320mg Q4W dosing arm, injections will be administered by study personnel using the ~~1mL PFS~~**investigational device** at Week 4 and Week 12; for subjects in both dosing arms, injections will be administered by study personnel using the **investigational device** ~~1mL PFS~~at Week 16. ~~After Week 16 in the DV0002 substudy, subjects will continue in PS0014 (the next visit after DV0002 completion will be the Week 20 Visit in PS0014).~~

First treatment for the 1ml device cohort in PS0014 will be the timepoint of first bimekizumab injection in DV0002. First treatment in DV0002 will be the timepoint of first self-injection in DV0002.

After Week 16 in the DV0002 substudy, subjects will continue in PS0014 (the next visit after DV0002 completion will be the Week 20 Visit in PS0014).

Change #12

Section 2.3.6 Planned number of subjects

It is planned to enroll approximately 200 subjects; each device arm will consist of approximately 100 subjects. It is anticipated that this study will involve up to 80 sites in North America.

Has been changed to:

For evaluation of the 1mL device, it ~~It~~ is planned to enroll approximately 200 subjects; each device arm **(bimekizumab-SS-1mL, bimekizumab-AI-1mL)** will consist of approximately 100 subjects.

Once the 1mL device cohort has finished enrolling, the 2mL device cohort will start enrolling. For evaluation of the 2mL device, it is planned to enroll approximately 100 subjects; each device arm (bimekizumab SS 2mL or bimekizumab-AI-2mL) will consist of approximately 50 subjects.

It is anticipated that this study will involve up to 80 sites in North America.

Change #13

Section 2.4 Determination of sample size

This study will not be powered with respect to any endpoint and sample size is based on practical considerations. In order to maintain blinding in the PS0014 feeder studies, DV0002 will recruit subjects who were administered bimekizumab 320mg (Q4W or Q8W) and subjects who were administered placebo or ustekinumab in the PS0014 feeder studies. A total of 100 subjects (50 subjects per device arm) are planned for PK trough level analyses, but these analyses can only be performed on subjects who do not change their bimekizumab dose or dosing regimen (ie, 320mg bimekizumab Q4W or Q8W) between the PS0014 feeder studies and the DV0002 substudy. The DV0002 substudy will therefore enroll approximately 200 subjects (to compensate for subjects with bimekizumab dose changes) to ensure that 100 subjects are available for PK trough analysis.

Each device arm will consist of approximately 100 subjects. Within each device arm, subjects will be divided into tertiles by BMI; there will be approximately 33 subjects per tertile, which is expected to yield approximately 16 to 17 subjects per tertile who are evaluable for steady state trough PK level analyses.

Subjects are evaluable for steady state trough PK level analyses, if they enter PS0014 on the same drug and dose as completing the feeder study and if they receive the drug at least 16-20 weeks before PS0014. The second condition is automatically fulfilled. Each subject in the feeder study will receive more than 20 week the same treatment in the maintenance phase except escape subjects from PS0013 which are excluded from DV0002 enrollment.

Has been changed to:

This study will not be powered with respect to any endpoint and sample size is based on practical considerations. **For the 1mL device cohort,** ~~In order~~ to maintain blinding in the PS0014 feeder studies, DV0002 will recruit subjects who were administered bimekizumab 320mg (Q4W or Q8W) and subjects who were administered placebo or ustekinumab in the PS0014 feeder studies. A total of 100 subjects (50 subjects per device arm) are planned for PK trough level analyses, but

these analyses can only be performed on subjects who do not change their bimekizumab dose or dosing regimen (ie, 320mg bimekizumab Q4W or Q8W) between the PS0014 feeder studies and the DV0002 substudy. The DV0002 substudy will therefore enroll approximately 200 subjects (to compensate for subjects with bimekizumab dose changes) to ensure that 100 subjects are available for PK trough analysis.

Subjects who enroll in the DV0002 substudy 1mL device cohort will be randomly assigned to the bimekizumab SS 1mL or the bimekizumab AI 1mL device arms (each device arm will consist of approximately 100 subjects)~~Each device arm will consist of approximately 100 subjects~~. Within each device arm, subjects will be divided into tertiles by BMI; there will be approximately 33 subjects per tertile, which is expected to yield approximately 16 to 17 subjects per tertile who are evaluable for steady state trough PK level analyses.

Subjects are evaluable for steady state trough PK level analyses, if they enter PS0014 on the same drug and dose as completing the feeder study and if they receive the drug at least 16-20 weeks before PS0014. The second condition is automatically fulfilled. Each subject in the feeder study will receive more than 20 week the same treatment in the maintenance phase except escape subjects from PS0013 which are excluded from DV0002 enrollment.

Once the 1mL device cohort has finished enrolling, the 2mL device cohort will start enrolling. Subjects who participated in the 1mL device cohort of DV0002 are not eligible to enroll in the 2mL device cohort. For evaluation of the 2mL device, it is planned to enroll approximately 100 subjects. All 100 subjects will have been on a consistent bimekizumab dose regimen for at least 16 weeks, and thus all will be evaluable for the PK trough level analyses.

Subjects who enroll in the DV0002 substudy 2mL device cohort will be randomly assigned to the bimekizumab SS 2mL or the bimekizumab AI 2mL device arms (each device arm will consist of approximately 50 subjects). Within each device arm, subjects will be divided into tertiles by BMI; there will be approximately 16 to 17 subjects per tertile who are evaluable for steady state trough PK level analyses.

Change #14

Section 3.5.1 1mL Device Cohort

3.5.1 Enrolled Set

3.5.2 Safety Set

3.5.3 Full Analysis Set

3.5.4 Pharmacokinetic Per Protocol Set

Two different Pharmacokinetic Per Protocol Sets (PK-PPS) will be generated (1 for each device type): the bimekizumab-SS-1mL PK-PPS (PK-PPS-s) and the bimekizumab-AI-1mL PK-PPS (PK-PPS-a). Each PK-PPS will consist of all subjects who receive the same bimekizumab administration (frequency and dose) in the PS0014 feeder studies as in the DV0002 substudy and who have at least 1 evaluable PK assessment in the DV0002 substudy without important protocol deviations that would affect the concentration. Pharmacokinetic variables will be analyzed using the PK-PPS-s and PK-PPS-a.

Has been changed to:

~~3.5.1~~**3.5.1.1** Enrolled Set

~~3.5.1~~**3.5.1.2** Safety Set

~~3.5.1~~**3.5.1.3** Full Analysis Set

~~3.5.1~~**3.5.1.4** Pharmacokinetic Per Protocol Set

Two different Pharmacokinetic Per Protocol Sets (PK-PPS) will be generated (1 for each device type): the bimekizumab-SS-1mL PK-PPS (PK-PPS-s) and the bimekizumab-AI-1mL PK-PPS (PK-PPS-a). Each PK-PPS will consist of all subjects who receive the same bimekizumab administration (frequency and dose) in the PS0014 feeder studies as in the DV0002 substudy and who have at least 1 evaluable PK assessment in the DV0002 substudy without important protocol deviations that would affect the concentration. Pharmacokinetic variables will be analyzed using the PK-PPS-s and PK-PPS-a.

All PK assessments after baseline assessments from feeder study will be considered for the requirement of at least one evaluable PK assessment.

Change #15

The following sections has been added:

3.5.2 2mL Device Cohort

3.5.2.1 Enrolled Set

The Enrolled Set (ES) will consist of all subjects who have given informed consent for DV0002.

3.5.2.2 Safety Set

Two different Safety Sets (SS) will be generated (1 for each device type): the bimekizumab-SS-2mL Safety Set (SS-s) and the bimekizumab-AI-2mL Safety Set (SS-a). Each SS will consist of all subjects in the study who receive at least 1 dose of bimekizumab by the indicated self-injection investigational device. Safety variables will be analyzed using the SS-s and SS-a.

3.5.2.3 Full Analysis Set

Two different Full Analysis Sets (FASs) will be generated (1 for each device type): FAS-s and FAS-a. Each FAS will consist of all subjects in the SS-s or SS-a who self-inject at least 1 dose of bimekizumab using the given device and who have an assessment of self-injection. All self-injection related endpoints will be analyzed using the FAS-s and FAS-a.

3.5.2.4 Pharmacokinetic Per Protocol Set

Two different Pharmacokinetic Per Protocol Sets (PK-PPS) will be generated (1 for each device type): the bimekizumab-SS-2mL PK-PPS (PK-PPS-s) and the bimekizumab-AI-2mL PK-PPS (PK-PPS-a). Each PK-PPS will consist of all subjects who receive the same bimekizumab administration (frequency and dose) in the PS0014 feeder studies as in the DV0002 substudy and who have at least 1 evaluable PK assessment in the DV0002 substudy without important protocol deviations that would affect the concentration. Pharmacokinetic variables will be analyzed using the PK-PPS-s and PK-PPS-a.

All PK assessments after baseline assessments from feeder study will be considered for the requirement of at least one evaluable PK assessment.

Change #16

Section 3.6 Treatment assignment, treatment and device groups

The PS0014 treatment groups are as follows:

- Bimekizumab 320mg Q4W
- Bimekizumab 320mg Q8W.

DV0002 device groups

This refers to the study device assigned to the subject at the beginning of DV0002. The DV0002 device groups are as follows:

- Bimekizumab-SS-1mL
- Bimekizumab-AI-1mL.

Has been changed to:

The PS0014 treatment groups are as follows:

- Bimekizumab 320mg ~~Q4W~~**Q8W**
- Bimekizumab 320mg ~~Q8W~~**Q4W**.

DV0002 device groups

This refers to the study device assigned to the subject at the beginning of DV0002. The DV0002 **1mL** device groups are as follows:

- Bimekizumab-SS-1mL
- Bimekizumab-AI-1mL.

The DV0002 2mL device groups are as follows:

- **Bimekizumab-SS-2mL**
- **Bimekizumab-AI-2mL.**

Change #17

Section 3.9 Changes to protocol-defined analyses

The following part has been removed:

~~The analysis sets to be used for the PK data have been amended from the PK Analysis set to the PK Per Protocol Analysis set (PK-PPS) throughout which will allow the exclusion of subjects with important protocol deviations related to PK from the primary analysis.~~

Change #18

Section 4.2 Handling of dropouts or missing data

If the intensity of an ADE is unknown, it will be considered as severe. If the relationship to study drug is missing, it is considered as related.

Has been changed to:

If the intensity of an ADE is unknown, it will be considered as severe. ~~If the relationship to study drug is missing, it is considered as related~~.

Change #19

Section 4.3 Interim analyses and data monitoring

The following part has been added:

The subjects of DV0002 are ongoing subjects of PS0014. Data cut off for the 1mL final analysis will be last subject last Week 16 visit in DV0002 in the 1mL device cohort. Data cut off for the 2mL final analysis will be last subject last Week 16 visit in DV0002 in the 2mL device cohort. Data cut off rules will be applied for ongoing adverse device events and ongoing concomitant medication.

Change #20

Section 5.1 Subject disposition

All subject disposition tables will use the PS0014 treatment groups BKZ 320mg Q4W and BKZ 320mg Q8W and an overall treatment group category (BKZ Total).

[…]

The number and percentage of subjects who entered the substudy, completed, discontinued with the reasons for discontinuation of the substudy will be presented. This summary will be based on the ES and will present all bimekizumab treated subjects by PS0014 treatment group and broken out by DV0002 device group.

Has been changed to:

All subject disposition tables will use the PS0014 treatment groups BKZ 320mg ~~Q4W~~ **Q8W** and BKZ 320mg ~~Q8W~~ **Q4W** and an overall treatment group category (BKZ Total).

[…]

The number and percentage of subjects who entered the substudy, completed, discontinued with the reasons for discontinuation of the substudy will be presented. This summary will be based on the ES and will present all bimekizumab treated subjects by PS0014 treatment group and broken out by DV0002 device group.

Subjects will be counted as completer if they completed the DV0002 Week 16 visit.

Change #21

Section 6.1. Demographics

Demographic variables will be summarized by PS0014 treatment group and all bimekizumab treated subjects.

The following continuous variables will be summarized using descriptive statistics (number of subjects, mean, SD, minimum, median and maximum).

- Age at the time of DV0002 study entry (years)
- Height (cm)
- Weight (kg)
- BMI (kg/m2)
- BMI (kg/m2) will be calculated as:

$$BMI = \frac{\text{Weight (kg)}}{(\text{Height (m)})^2}$$

The following categorical variables will be summarized using frequency counts and percentages.

- Age group (≤18, 19-<65, ≥65 years)
- Body Weight (≤100kg, >100kg)
- BMI (<25 kg/m2, 25 to <30 kg/m2, ≥30 kg/m2)
- BMI tertiles (≤t1 kg/m2, >t1 kg/m2 to ≤ t2 kg/m2, >t2 kg/m2) based on the respective PK-PPS populations (PK-PPS-s, PK-PPS-s)

Has been changed to:

Demographic variables will be summarized by PS0014 treatment group and all bimekizumab treated subjects.

The following continuous variables will be summarized using descriptive statistics (number of subjects, mean, SD, minimum, median and maximum).

- Age at the time of ~~DV0002~~**feeder** study entry (years)
- Height (cm)
- **DV0002 Baseline** Weight (kg)**: will be derived from the weight from the last visit of the feeder study for 1mL device cohort subjects and will be derived from last weight prior to first treatment in DV0002 for 2mL cohort**
- **DV0002 Baseline** BMI (kg/m2)
- BMI (kg/m2) will be calculated as:

$$BMI = \frac{\text{Weight (kg)}}{(\text{Height (m)})^2}$$

The following categorical variables will be summarized using frequency counts and percentages.

- Age group (≤18, 19-<65, ≥65 years)
- **DV0002 Baseline** Body Weight (≤100kg, >100kg)
- BMI (<25 kg/m2, 25 to <30 kg/m2, ≥30 kg/m2)
- BMI tertiles (≤t1 kg/m2, >t1 kg/m2 to ≤ t2 kg/m2, >t2 kg/m2) based on the respective PK-PPS populations (PK-PPS-s, PK-PPS-s)

Change #22

Section 6.2 Other Baseline characteristics

$$\text{Disease Duration} = \frac{(\text{Date of randomization} - \text{Date of onset of Plaque Psoriasis}^{1})}{365.25}$$

Has been changed to:

$$\text{Disease Duration} = \frac{(\text{Date of randomization } \mathbf{in\ DV0002} - \text{Date of onset of Plaque Psoriasis}^{1})}{365.25}$$

Change #23

Section 6.3 Medical history and concomitant diseases

All medical conditions not yet occurred and reported in the feeder studies will be presented in a by-subject listing for SS-s and SS-a, respectively.

Has been changed to:

Previous and ongoing medical history from feeder study will be based on SS-s and SS-a and summarized by treatment groups, system organ class (SOC) and preferred term (PT) using MedDRA®. Medical history and psoriasis history will be included in the summary tables and listings for medical history. Medical procedures are not coded.

Previous and ongoing medical history ~~All medical conditions not yet occurred and reported in the feeder studies~~ will be presented in a by-subject listing for SS-s and SS-a, respectively.

Change #24

Section 6.4 Prior and concomitant medications

Concomitant medication details are collected at each visit of DV0002. Concomitant medications are medications taken at least one day in common with the PS0014 study medication dosing period (Baseline to Visit 16).

No imputation of start and stop dates will be done for concomitant medication. If a date is missing the medication is assumed to be concomitant.

All concomitant medication will be listed for SS-s and SS-a, respectively.

Has been changed to:

Concomitant medication details are collected at each visit of DV0002. Concomitant medications are medications taken at least one day in common with the ~~PS0014~~ **DV0002** study medication dosing period (**DV0002** Baseline to ~~Visit~~ **DV0002 Week** 16).

No imputation of start and stop dates will be done for concomitant medication. If a date is missing the medication is assumed to be concomitant.

All concomitant medication will be listed for SS-s and SS-a, respectively.

Concomitant medication which started before DV0002 Week 16 and were ongoing at the data cut off will be included with the status remaining as ongoing. Concomitant medication which were ongoing at DV0002 Week 16 but with an end date before the data cut off will be included with their end date as recorded.

Change #25

Section 9.1 Pharmacokinetics

The statistical analyses of the PK data will be descriptive in nature and will be summarized using the relevant device-specific population (PK-PPS-s or PK-PPS-a). Data will be analyzed overall for each device by injection type (self-administered or study personnel-administered), by injection site (abdomen or thigh), and by BMI category. The BMI categories will be defined into three tertiles within each device arm PK-PPS analysis set and derived from subjects' Baseline BMI values.

To allow for an analysis of PK trough levels for bimekizumab administration via self-injection or via study personnel administration, pre-dose PK samples will be taken throughout the DV0002 substudy. For the Q4W dose regimen, PK trough levels will be determined based on pre-dose PK sampling at Baseline and Week 8 for the study personnel administration and at Week 4 and Week 12 for the self-administration trough levels, respectively. For the Q8W dose regimen, PK trough levels will be determined based on pre-dose PK sampling at Baseline for the study personnel administration and at Week 8 and Week 16 for the self-administration trough levels, respectively. For the analysis of PK trough levels by injection site (abdomen or thigh) and by BMI category (by tertile), only self-administration PK trough levels will be used.

PK summaries will be based on observed values. No imputation will be used. However, if plasma concentration measurements are below the level of quantification, then for calculation of the derived statistics the result will be set to ½ of the lower level of quantification (LLOQ). Descriptive statistics including geometric mean, geometric coefficient of variation, and geometric mean 95% CI if applicable will be calculated if at least 2/3 of the values of interest are above the LLOQ. If this is not the case, only median, minimum, and maximum will be presented.

Boxplots of plasma concentration will be presented by visit and by treatment group.

Has been changed to:

The statistical analyses of the PK data will be descriptive in nature and will be summarized using the relevant device-specific population (PK-PPS-s or PK-PPS-a). Data will be analyzed overall for each device by injection type (self-administered or study personnel-administered), by injection site (abdomen or thigh), and by BMI category. The BMI categories will be defined into three tertiles within each device arm PK-PPS analysis set **and device cohort** and derived from subjects' **DV0002** Baseline BMI values.

To allow for an analysis of PK trough levels for bimekizumab administration via self-injection or via study personnel administration, pre-dose PK samples will be taken throughout the DV0002 substudy. For the Q4W dose regimen, PK trough levels will be determined based on pre-dose PK sampling at **DV0002** Baseline and **DV0002** Week 8 for the study personnel administration and at **DV0002** Week 4 and **DV0002** Week 12 for the self-administration trough levels, respectively. For the Q8W dose regimen, PK trough levels will be determined based on pre-dose PK sampling at **DV0002** Baseline for the study personnel administration and at **DV0002** Week 8 and **DV0002** Week 16 for the self-administration trough levels, respectively. **For the 1ml device cohort, DV0002 Baseline PK samples are the PK samples from the last visit of the feeder studies.**

For the analysis of PK trough levels by injection site (abdomen or thigh) and by BMI category (by tertile**s**), ~~only~~ self-administration PK trough levels **and study personnel administration PK trough levels** will be used.

In case the injection sites are different for both injections at one visit, or the injection site is the arm (not abdomen or thigh) the PK results will not be included for the summary by injection site.

PK samples for self-administration where the injection was done by site personnel or caregiver will be listed but not be used for summary statistics. PK samples for personnel administration where the injection was done by the subject will be listed but not be used for summary statistics.

Only pre-dose (trough) concentrations will be included while summarizing tables and figures. If the dosing for a visit is +/- 7 days out of window then the plasma concentration from that visit and all subsequent visits will be excluded from the PK summary. PK samples collected after dosing will be excluded from summary statistics.

PK summaries will be based on observed values. No imputation will be used. However, if plasma concentration measurements are below the level of quantification, then for calculation of the derived statistics the result will be set to ½ of the lower level of quantification (LLOQ). Descriptive statistics including geometric mean, geometric coefficient of variation, and geometric mean 95% CI if applicable will be calculated if at least 2/3 of the values of interest are above the LLOQ. If this is not the case, only median, minimum, and maximum will be presented.

Boxplots of plasma concentration will be presented by visit and by treatment group.

All PK results will be listed.

In addition, the PK results from all subjects not in PK-PPS-s or PK-PPS-a will be listed based on the SS-a and SS-s.

Change #26

Section 10.2 Adverse events

10.1.1 Adverse device effects

All AEs (including serious adverse events [SAEs]) will be reported in a common database for PS0014 and DV0002, but only adverse device effects (ADEs), serious adverse device effects (SADEs), and device deficiencies will be summarized in the DV0002 substudy. Specifically, only those AEs related to the use of the investigational medical devices bimekizumab-SS-1mL or bimekizumab-AI-1mL (based on the Investigator's judgement) will be assessed. All AEs (including SAEs) which are not assessed to be related to the investigational devices will be summarized separately in the report for the main study PS0014.

[…]

- Incidence of TEADEs leading to discontinuation

For definition of serious, unanticipated and serious unanticipated ADEs see protocol of DV0002.

Has been changed to:

~~10.1.1 Adverse device effects~~

All AEs (including serious adverse events [SAEs]) will be reported in a common database for PS0014 and DV0002, but only adverse device effects (ADEs), serious adverse device effects (SADEs), and device deficiencies will be summarized in the DV0002 substudy. Specifically, only those AEs related to the use of the investigational medical devices bimekizumab-SS-1mL or bimekizumab-AI-1mL (based on the Investigator's judgement) will be assessed. All AEs (including SAEs) which are not assessed to be related to the investigational devices will be summarized separately in the report for the main study PS0014. **An exception are AEs that are indicated as injection site reactions during self-injection. These will be listed in DV0002 as well as in PS0014.**

10.2.1 Adverse device effects

[…]

- Incidence of TEADEs leading to discontinuation
- **Incidence of non-TEADEs (only listed and not summarized in a table)**

For definition of serious, unanticipated and serious unanticipated ADEs see protocol of DV0002.

Adverse device effects which started before DV0002 Week 16 and were ongoing at the data cut off will be included with the status remaining as ongoing. Adverse device effects which were ongoing at DV0002 Week 16 but with an end date before the data cut off will be included with their end date as recorded.

10.2.2 Injection site reaction

Injection site reactions are recorded at the AE CRF page at the time when they occur. All AEs will be coded and classified by system organ class, high level term, and preferred term. An AE with High Level Terms of "Administration site reactions NEC" and "Injection site reactions" will be evaluated as injection site reaction.

All injection site reactions for self-injection with a start date on or following the first self-administration of study treatment through the final self-administration of study treatment + 7 days will be listed.

Change #27

Section 11.1 Primary outcome

The primary outcome variable is the percentage of all subjects able to self-administer safe and effective injections using the given device at Week 8. Safe and effective self-injection will be evaluated by the study personnel as defined below:

- Complete dose delivery: Subject self-injects the complete dose of bimekizumab as confirmed by a visual inspection of the bimekizumab-SS-1mL or the bimekizumab-AI-1mLinvestigational device which shows that the IMP is delivered completely (ie, container is empty), and
- No ADEs that would preclude continued use of the device for self-injection (ie, no SADEs and/or ADEs leading to withdrawal from the DV0002 substudy).

All data to assess the primary outcome is collected on the subject self-injection of bimekizumab CRF page for Week 8. For the number of subjects with safe and effective self-injections simply

the cases which indicated "yes" for the question "Did the subject self-inject the complete dose of Bimekizumab" and "no" for the question "Where there any AEs related to use of the investigational device for self-injection" at Week 8 are counted.

Two self-injections will be performed at Week 8 and the questions will be answered twice. If the answers are different between both self-injections in one visit, then the worst case of both answers will be used for analysis at this visit.

[…]

Has been changed to:

The primary outcome variable is the percentage of all subjects able to self-administer safe and effective injections using the given device at **DV0002** Week 8. Safe and effective self-injection will be evaluated by the study personnel as defined below:

- Complete dose delivery: Subject self-injects the complete dose of bimekizumab as confirmed by a visual inspection of the ~~bimekizumab-SS-1mL or the bimekizumab-AI-1mL~~**investigational device** which shows that the IMP is delivered completely (ie, container is empty), and
- No ADEs that would preclude continued use of the device for self-injection (ie, no SADEs and/or ADEs leading to withdrawal from the DV0002 substudy).

All data to assess the primary outcome is collected on the subject self-injection of bimekizumab CRF page for **DV0002** Week 8. For the number of subjects with safe and effective self-injections simply the cases which indicated "yes" for the question "Did the subject self-inject the complete dose of Bimekizumab" and "no" for the question "Where there any AEs related to use of the investigational device for self-injection" at **DV0002** Week 8 are counted.

For subjects in the 1mL device cohort, ~~T~~two self-injections will be performed at **DV0002** Week 8 and the questions will be answered twice. If the answers are different between both self-injections in one visit, then the worst case of both answers will be used for analysis at this visit. **Subjects with only one self-injection at one visit will be counted as non-responder. Assessments where the self-injection was not performed by the subject will be not included in any summary statistics.**

[…]

Change #28

Section 11.2 Secondary outcome

The secondary outcome variable is the percentage of subjects able to self-administer safe and effective injections using the given device at Baseline (first self-injection visit). Safe and effective self-injection will be evaluated by the study personnel. The secondary outcome variables will be analyzed in the same manner as the primary outcome variable. All data to assess the secondary outcome is collected on Subject self-injection of Bimekizumab CRF page for Baseline.

Has been changed to:

The secondary outcome variable is the percentage of subjects able to self-administer safe and effective injections using the given device at **DV0002** Baseline (first self-injection visit). Safe and effective self-injection will be evaluated by the study personnel. The secondary outcome variables will be analyzed in the same manner as the primary outcome variable. All data to assess the secondary outcome is collected on Subject self-injection of Bimekizumab CRF page for **DV0002** Baseline.

Change #29

Section 11.3 Other outcomes

The secondary outcome variables will be summarized using descriptive statistics and they will be tabulated separately for each device overall based and within each device by PS0014 treatment.

Has been changed to:

The ~~secondary~~ **other** outcome variables will be summarized using descriptive statistics and they will be tabulated separately for each device overall based and within each device by PS0014 treatment.

Assessments where the self-injection was not performed by the subject will be not included in any summary statistics.

Change #30

Section 11.3.1 Pre-injection SIAQ (versions 2.0 and 2.1)

The pre-injection SIAQ (versions 2.0 and 2.1) will be performed at Baseline. Version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL and version 2.1 of the SIAQ will be used to assess bimekizumab-AI-1mL. There are no differences in Version 2.0 to Version 2.1 in pre-injection SIAQ.

The pre-injection SIAQ consists of 7 items each with a scale of 1 to 5. There is an overall score (7 items) and three individual subscales (feelings about injections [FL, 3 items], self-confidence [CO, 3 items] and satisfaction with current mode of administration [SA, 1 item]). Each subscale and the overall score will be calculated using the average of the individual transformed item scores. The item score will be transformed using the following rule:

$$Transformed\ Item\ Score = \big((raw\ item\ score) - 1\big) \times 2.5$$

In the case of missing values, no domain score will be calculated if more than 50% of the items within the domain are missing.

Higher individual or overall total scores of the pre- -injection indicate more confidence, higher satisfaction and less concerns with self-injections.

Summary statistics for all individual items, each subscale and the total score will be produced for Baseline.

Has been changed to:

The pre-injection SIAQ (versions 2.0 and 2.1) will be **completed** ~~performed~~ at **DV0002** Baseline. Version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL **and bimekizumab-SS-2mL** and version 2.1 of the SIAQ will be used to assess bimekizumab-AI-

1mL **and bimekizumab-AI-2mL**. There are no differences in Version 2.0 to Version 2.1 in pre-injection SIAQ.

The pre-injection SIAQ consists of 7 items each with a scale of 1 to 5. ~~There is an overall score (7 items) and~~ **There are** three individual subscales (feelings about injections [FL, 3 items], self-confidence [CO, 3 items] and satisfaction with current mode of administration [SA, 1 item]). Each subscale **score** ~~and the overall score~~ will be calculated using the average of the individual transformed item scores. The item score will be transformed using the following rule:

Transformed Item Score= ((raw item score)-1) × 2.5

In the case of missing values, no domain score will be calculated if more than 50% of the items within the domain are missing.

Higher individual ~~or overall total~~ scores of the pre-~~-~~injection **SIAQ** indicate more confidence, higher satisfaction and less concerns with self-injections.

Summary statistics for all individual items **and** ~~,~~ each subscale ~~and the total score~~ will be produced for Baseline.

Change #31

Section 11.3.2 Post-injection SIAQ (versions 2.0 and 2.1)

The post-injection SIAQ (versions 2.0 and 2.1) will be performed at Baseline. Version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL and version 2.1 of the SIAQ will be used to assess bimekizumab-AI-1mL. Version 2.0 and version 2.1 of the SIAQ are identical, except for Question 11 due to different handling of the devices.

The post-injection SIAQ consists of 21 items on 6 individual subscales (FL [3 items], self-image [IM, 1 item], CO [3 items], Injection-site reactions [RE, 2 items], ease of use [EU, 5 items) and satisfaction with self-injection [SA, 3 items]). The items of the individual subscale SA have a score range of 1 to 6, the other individual subscales have a score range of 1 to 5. Each subscale and the overall score will be calculated using the average of the individual transformed item scores. The item scores for the SA subscale will be transformed using the following rule:

Transformed Item Score= ((raw item score)-1) × 2

The item scores for the other subscales and the overall score will be transformed using the following rule:

Transformed Item Score= ((raw item score)-1) × 2.5

In the case of missing values, no domain score will be calculated if more than 50% of the items within the domain are missing.

Higher individual or overall total scores of the post-injection indicate more confidence, higher satisfaction and less concerns with self-injections.

Summary statistics for all individual items, each subscale and the total score will be produced for Baseline and week 8.

Has been changed to:

The post-injection SIAQ (versions 2.0 and 2.1) will be **completed** ~~performed~~ at **DV0002** Baseline **and DV0002 Week 8**. Version 2.0 of the SIAQ will be used to assess bimekizumab-

SS-1mL **and bimekizumab-SS-2mL** and version 2.1 of the SIAQ will be used to assess bimekizumab-AI-1mL **and bimekizumab-AI-2mL**. Version 2.0 and version 2.1 of the SIAQ are identical, except for Question 11 due to different handling of the devices.

The post-injection SIAQ consists of 21 items on 6 individual subscales (FL [3 items], self-image [IM, 1 item], CO [3 items], Injection-site reactions [RE, 2 items], ease of use [EU, 5 items) and satisfaction with self-injection [SA, 7 items]). The items of the individual subscale ~~SA~~ **EU** have a score range of 1 to 6, the other individual subscales have a score range of 1 to 5. Each subscale **score** ~~and the overall score~~ will be calculated using the average of the individual transformed item scores. The item scores for the ~~SA~~ **EU** subscale will be transformed using the following rule:

$$\text{Transformed Item Score} = ((\text{raw item score}) - 1) \times 2$$

The item scores for the other subscales ~~and the overall score~~ will be transformed using the following rule:

$$\text{Transformed Item Score} = ((\text{raw item score}) - 1) \times 2.5$$

In the case of missing values, no domain score will be calculated if more than 50% of the items within the domain are missing.

Higher individual ~~or overall total~~ scores of the post-injection **SIAQ** indicate more confidence, higher satisfaction and less concerns with self-injections.

Summary statistics for all individual items **and** each subscale ~~and the total score~~ will be produced for **DV0002** Baseline and **DV0002** ~~w~~**W**eek 8.

Change #32

Section 11.3.3 Injection site pain

The visual analog scale of injection site pain indicates the level of pain during the injection. It reaches from 0-100 mm with higher values for more severe pain and 0 for no pain.

Summary statistics of actual values and change from Baseline values will be used to summarize injection site pain by visit after self-injection.

Has been changed to:

The visual analog scale of injection site pain indicates the level of pain during the injection. It **ranges** ~~reaches~~ from 0-100 mm with higher values **indicating** ~~for~~ more severe pain and 0 for no pain.

Summary statistics of actual values and change from **DV0002** Baseline values will be used to summarize injection site pain by visit after self-injection.

Change #33

Section 11.3.4 Structural and mechanical integrity of the devices

Frequency tables will be produced to show the number and percentage of devices with:

- used bimekizumab-SS-1mL and bimekizumab-AI-1mL syringes identified as having structural integrity issues after completion of self-injection.

- used bimekizumab-SS-1mL and bimekizumab-AI-1mL syringes identified as functionally compromised.

Has been changed to:

Frequency tables will be produced to show the number and percentage of devices with:

- used bimekizumab-SS-1mL**, bimekizumab-AI-1mL, bimekizumab-SS-2mL** and bimekizumab-AI-~~1mL~~**2mL** syringes identified as having structural integrity issues after completion of self-injection.
- used bimekizumab-SS-1mL**, bimekizumab-AI-1mL, bimekizumab-SS-2mL** and bimekizumab-AI-~~1mL~~**2mL** syringes identified as functionally compromised.

The 90% CIs based on the Exact Binomial method will be reported as well.

13.2 SAP Amendment 2

Rationale for the amendment

It was decided to add the analysis of the COVID-19 impact for the 2mL phase analysis.

Modifications and changes

Global changes:

The following changes were made throughout the SAP:

- The list of abbreviations was updated accordingly.
- Minor spelling, editorial, and formatting changes were made throughout the document.

Specific changes

In addition to the global changes, the following specific changes have been made (formats as missing spaces or redundant spaces are not listed):

Change #1

The following sections has been added:

3.2 Analysis Time Points

If the early withdrawal visit occurs at a scheduled visit as outlined in the schedule of assessments, then no mapping is necessary, and any early withdrawal assessments should correspond to that scheduled visit. Premature study withdrawal visit assessments that occur on a date after a scheduled visit will be assigned to the next scheduled site visit per the protocol following the last visit where assessments were available.

Change #2

The following paragraphs have been added to section 3.5 Protocol deviations:

WHO declared a global COVID-19 pandemic on 11 March 2020. All subjects were recruited into this study during the pandemic and therefore the impact of COVID-19 on the study will be assessed. Deviations related to the Coronavirus Disease 2019 (COVID-19) global pandemic are unavoidable deviations from the protocol due to confirmed COVID-19

infection, suspected COVID-19 infection, general circumstances around COVID-19 without infection or any other deviation from the protocol due to COVID-19. COVID-19 protocol deviations will be reviewed as part of the ongoing data cleaning process. Any COVID-19 impact protocol deviations that are determined to be important or not-important will be included in this summary. A by-subject listing of COVID-19 related protocol deviations will be provided.

Change #3

The following sections has been added:
3.10.1 Changes related to COVID-19
COVID-19 protocol deviations have been defined in Section 3.5 and the presentation of COVID-19 protocol deviations is described in Section 5.3.

Change #4

Section 4.2 Handling of dropouts or missing data

For analyses of ADEs and concomitant medication usage, a complete date must be established in order to correctly identify the ADE or medication as occurring during treatment or not. For purposes of imputing missing components of partially-reported start and stop dates for ADEs, for medication use, the algorithms listed below will be followed. Start and stop dates of ADEs or concomitant medication will be displayed as reported in the subject data listings (i.e., no imputed values will be displayed in data listings).

Partial ADE and concomitant medication start dates will be imputed as follows:

Imputation of Partial Start Dates

- If only the month and year are specified and the month and year of first dose is not the same as the month and year of the start date, then use the 1st of the month
- If only the month and year are specified and the month and year of first dose is the same as the month and year of the start date, then use the date of first dose
- If only the year is specified, and the year of first dose is not the same as the year of the start date, then use the 1st of January of the year of the start date
- If only the year is specified, and the year of first dose is the same as the year of the start date, then use the date of first dose
- If the start date is completely unknown and the stop date is unknown or not prior to the date of first dose, then use the date of first dose.

Imputation of Partial Stop Dates

- If only the month and year are specified, then use the last day of the month
- If only the year is specified, then use December 31st of that year
- If the stop date is completely unknown, do not impute the stop date.

Has been changed to:

For analyses of ADEs and concomitant medication usage, a complete date must be established in order to correctly identify the ADE or medication as occurring during treatment or not. **To calculate the duration of disease, a complete date of onset of plaque psoriasis is needed.** For purposes of imputing missing components of partially-reported start and stop dates for ADEs, for medication use, **and date of onset of plaque psoriasis,** the algorithms listed below will be

followed. Start and stop dates of ADEs or concomitant medication will be displayed as reported in the subject data listings (i.e., no imputed values will be displayed in data listings).

Partial ADE and concomitant medication start dates will be imputed as follows:

Imputation of Partial Start Dates

- If only the month and year are specified and the month and year of first dose is not the same as the month and year of the start date, then use the 1st of the month
- If only the month and year are specified and the month and year of first dose is the same as the month and year of the start date, then use the date of first dose
- If only the year is specified, and the year of first dose is not the same as the year of the start date, then use the 1st of January of the year of the start date
- If only the year is specified, and the year of first dose is the same as the year of the start date, then use the date of first dose
- If the start date is completely unknown and the stop date is unknown or not prior to the date of first dose, then use the date of first dose.

Imputation of Partial Stop Dates

- If only the month and year are specified, then use the last day of the month
- If only the year is specified, then use December 31st of that year
- If the stop date is completely unknown, do not impute the stop date.

If the (imputed) stop date is prior to the imputed start date:

- **If only the month and year are specified and the month and year of first dose is the same as the month and year of the start date and the stop date is before the date of first dose, then set the start date to the 1st of that month.**
- **If only the year is specified, and the year of first dose is the same as the year of the start date, and the stop date is before the date of first dose, then use the 1st of January of the year of the start date**

Partial start dates for onset date of plaque psoriasis will be imputed as follows:

- **If only the month and year are specified, then use the last day of the month.**
- **If only the year is specified, then use the 31st of December of the year.**
- **If the start date is completely unknown, do not impute the start date.**

Change #5

The following section is added:

Section 5.3 COVID-19 Impact

For study participants impacted by the COVID-19 global pandemic, data was collected on a separate eCRF. This form was collected for study visits that were affected by COVID-19, and it collected how the visits were impacted by the pandemic (e.g., performed out of window, done by telephone instead of on-site, not done, etc).

Based on how the visit was affected by the global pandemic, all visits will have a variable indicating how the visit was performed:

- **Visit not done at all**
- **Visit done by video call**
- **Visit done by telephone**
- **Visit done at different time point than planned / out of window**

Additionally, for visits that are affected by COVID-19, all assessments that are missing will be flagged as missing due to COVID-19. Further, the specific reason of missing data will be captured as the following flags:

- **Confirmed COVID-19 infection**
- **Suspected COVID-19 infection**
- **General circumstances around COVID-19 without infection**
- **Other**

A summary of number and percentage of subjects with COVID-19 related protocol deviations and COVID-19 related device protocol deviations by treatment group and visit will be provided for the SS-a and SS-s. This summary on COVID-19 related protocol deviations will also be repeated by country.

A by-site, subject and visit listing of COVID-19 related protocol deviations along with a listing of COVID-19 related device protocol deviations will be provided.

Change #6

The following text in section 13.2 has been removed:

No imputation of start and stop dates will be done for concomitant medication. If a date is missing the medication is assumed to be concomitant.

Change #7

The following text in section 9.1 has been removed:

In case the injection sites are different for both injections at one visit, or the injection site is the arm (not abdomen or thigh) the PK results will not be included for the summary by injection site.

Change #8

The following text has been added to section 10.2.1 Adverse device effects:

Adverse events are recorded at the AE CRF page at the time when they occur. If an adverse event is related to the device by assessment of the investigator it is counted as an Adverse device event. **For DV0002 only ADE will be considered which started during the DV0002 study period. And ADEs started in the 1 ml phase will be included for 1 ml phase analysis, and those started in the 2 ml phase will be included for the 2 ml phase analysis.**

13.3 SAP Amendment 3

Rationale for the amendment

It was decided to update the PK-PPS definition for the 2mL phase analysis.

Modifications and changes

Global changes:

The following changes were made throughout the SAP:

- Minor spelling, editorial, and formatting changes were made throughout the document.

Specific changes

In addition to the global changes, the following specific changes have been made (formats as missing spaces or redundant spaces are not listed):

Change #1

The section 2.4 Determination of sample size:

This study will not be powered with respect to any endpoint and sample size is based on practical considerations. For the 1mL device cohort, to maintain blinding in the PS0014 feeder studies, DV0002 will recruit subjects who were administered bimekizumab 320mg (Q4W or Q8W) and subjects who were administered placebo or ustekinumab in the PS0014 feeder studies. A total of 100 subjects (50 subjects per device arm) are planned for PK trough level analyses, but these analyses can only be performed on subjects who do not change their bimekizumab dose or dosing regimen (ie, 320mg bimekizumab Q4W or Q8W) between the PS0014 feeder studies and the DV0002 substudy. The DV0002 substudy will therefore enroll approximately 200 subjects (to compensate for subjects with bimekizumab dose changes) to ensure that 100 subjects are available for PK trough analysis.

Subjects who enroll in the DV0002 substudy 1mL device cohort will be randomly assigned to the bimekizumab SS 1mL or the bimekizumab AI 1mL device arms (each device arm will consist of approximately 100 subjects). Within each device arm, subjects will be divided into tertiles by BMI; there will be approximately 33 subjects per tertile, which is expected to yield approximately 16 to 17 subjects per tertile who are evaluable for steady state trough PK level analyses.

Subjects are evaluable for steady state though PK level analyses, if they enter PS0014 on the same drug and dose as completing the feeder study and if they receive the drug at least 16-20 weeks before PS0014. The second condition is automatically fulfilled. Each subject in the feeder study will receive more than 20 week the same treatment in the maintenance phase except escape subjects from PS0013 which are excluded from DV0002 enrollment.

Once the 1mL device cohort has finished enrolling, the 2mL device cohort will start enrolling. Subjects who participated in the 1mL device cohort of DV0002 are not eligible to enroll in the 2mL device cohort. For evaluation of the 2mL device, it is planned to enroll approximately 100 subjects. All 100 subjects will have been on a consistent bimekizumab dose regimen for at least 16 weeks, and thus all will be evaluable for the PK trough level analyses.

Subjects who enroll in the DV0002 substudy 2mL device cohort will be randomly assigned to the bimekizumab SS 2mL or the bimekizumab AI 2mL device arms (each device arm will consist of approximately 50 subjects). Within each device arm, subjects will be divided into tertiles by BMI; there will be approximately 16 to 17 subjects per tertile who are evaluable for steady state trough PK level analyses.

Has been updated to:

This study will not be powered with respect to any endpoint and sample size is based on practical considerations.

1mL Device Cohort

For the 1mL device cohort, to maintain blinding in the PS0014 feeder studies, DV0002 will recruit subjects who were administered bimekizumab 320mg (Q4W or Q8W) and subjects who were administered placebo or ustekinumab in the PS0014 feeder studies. A total of 100 subjects (50 subjects per device arm) are planned for PK trough level analyses, but these analyses can only be performed on subjects who do not change their bimekizumab dose or dosing regimen (ie, 320mg bimekizumab Q4W or Q8W) between the PS0014 feeder studies and the DV0002 substudy. The DV0002 substudy will therefore enroll approximately 200 subjects (to compensate for subjects with bimekizumab dose changes) to ensure that 100 subjects are available for PK trough analysis.

Subjects who enroll in the DV0002 substudy 1mL device cohort will be randomly assigned to the bimekizumab SS 1mL or the bimekizumab AI 1mL device arms (each device arm will consist of approximately 100 subjects). Within each device arm, subjects will be divided into tertiles by BMI; there will be approximately 33 subjects per tertile, which is expected to yield approximately 16 to 17 subjects per tertile who are evaluable for steady state trough PK level analyses.

Subjects are evaluable for steady state t~~h~~**hr**ough PK level analyses, if they enter PS0014 on the same drug and dose as completing the feeder study and if they receive the drug at least 16-20 weeks before PS0014. The second condition is automatically fulfilled. Each subject in the feeder study will receive more than 20 week**s of** the same treatment in the maintenance phase except escape subjects from PS0013 which are excluded from DV0002 enrollment.

2mL Device Cohort

Once the 1mL device cohort has finished enrolling, the 2mL device cohort will start enrolling. Subjects who participated in the 1mL device cohort of DV0002 are not eligible to enroll in the 2mL device cohort. For evaluation of the 2mL device, it is planned to enroll approximately 100 subjects. Subjects are evaluable for steady state trough PK level analysis if they receive the same bimekizumab administration (frequency and dose) from ~~PS0014 feeder study as in the DV0002 substudy~~ **beginning of PS0014 through to the end of the sub-study**. **It is expected that most subjects will be evaluable for the PK trough level analyses.** ~~All 100 subjects will have been on a consistent bimekizumab dose regimen for at least 16 weeks, and thus all will be evaluable for the PK trough level analyses.~~

Subjects who enroll in the DV0002 substudy 2mL device cohort will be randomly assigned to the bimekizumab-SS-2mL or the bimekizumab-AI-2mL device arms (each device arm will consist of approximately 50 subjects). Within each device arm, subjects will be divided into

tertiles by BMI; there will be approximately 16 to 17 subjects per tertile who are evaluable for steady state trough PK level analyses.

Change #2

3.6.2.4 Pharmacokinetic Per Protocol Set

Two different Pharmacokinetic Per Protocol Sets (PK-PPS) will be generated (1 for each device type): the bimekizumab-SS-2mL PK-PPS (PK-PPS-s) and the bimekizumab-AI-2mL PK-PPS (PK-PPS-a). Each PK-PPS will consist of all subjects who receive the same bimekizumab administration (frequency and dose) in the PS0014 feeder studies as in the DV0002 substudy and who have at least 1 evaluable PK assessment in the DV0002 substudy without important protocol deviations that would affect the concentration. Pharmacokinetic variables will be analyzed using the PK-PPS-s and PK-PPS-a.

All PK assessments after baseline assessments from feeder study will be considered for the requirement of at least one evaluable PK assessment.

has been updated to:

Two different Pharmacokinetic Per Protocol Sets (PK-PPS) will be generated (1 for each device type): the bimekizumab-SS-2mL PK-PPS (PK-PPS-s) and the bimekizumab-AI-2mL PK-PPS (PK-PPS-a). Each PK-PPS will consist of all subjects who receive the same bimekizumab administration (frequency and dose) ~~in the PS0014 feeder studies~~ **from beginning of PS0014 through to the end of DV0002 substud**y ~~as in the DV0002 substudy~~ and who have at least 1 evaluable PK assessment in the DV0002 substudy without important protocol deviations that would affect the concentration. Pharmacokinetic variables will be analyzed using the PK-PPS-s and PK-PPS-a.

~~All PK assessments after baseline assessments from feeder study will be considered for the requirement of at least one evaluable PK assessment.~~

All PK assessments after DV0002 baseline assessments (Week 24, Week 28 or Week 32 from PS0014 study) will be considered for the requirement of at least one evaluable PK assessment.

Change #3

The section 6.3 Medical history and concomitant diseases

Previous and ongoing medical history from feeder study will be based on SS-s and SS-a and summarized by treatment groups, system organ class (SOC) and preferred term (PT) using MedDRA®. Medical history and psoriasis history will be included in the summary tables and listings for medical history. Medical procedures are not coded.

Previous and ongoing medical history will be presented in a by-subject listing for SS-s and SS-a, respectively.

Has been updated to:

6.3 Medical history and concomitant diseases

Previous and ongoing medical history **collected at the start of the** ~~from~~ feeder study will be based on SS-s and SS-a and summarized by treatment groups, system organ class (SOC) and

preferred term (PT) using MedDRA®. Medical history and psoriasis history will be included in the summary tables and listings for medical history. Medical procedures are not coded.

Previous and ongoing medical history **along with the updated medical history collected at the end of the feeder studies** will be presented in a by-subject listing for SS-s and SS-a, respectively.

Change #4

The following text is added to section 6.4 Prior and concomitant medications:

For 2 ml phase analysis, concomitant medications include those started on or before the later of the final contact date or (the last injection date + 7 days).

Change #5

Section 10.2.1 Adverse device effects:

Adverse events are recorded at the AE CRF page at the time when they occur. If an adverse event is related to the device by assessment of the investigator it is counted as an Adverse device event. For DV0002 only ADE will be considered which started during the DV0002 study period. And ADEs started in the 1 ml phase will be included for 1 ml phase analysis, and those started in the 2 ml phase will be included for the 2 ml phase analysis.

Has been updated to:

Adverse events are recorded at the AE CRF page at the time when they occur. If an adverse event is related to the device by assessment of the investigator it is counted as an Adverse device event. For DV0002 only ADE will be considered which started during the DV0002 study period. And ADEs started in the 1 ml phase will be included for 1 ml phase analysis, and those started in the 2 ml phase will be included for the 2 ml phase analysis. **For 2 ml phase analysis, adverse device effects include those started on or before the later of the final contact date or (the last injection date + 7 days).**

STATISTICAL ANALYSIS PLAN SIGNATURE PAGE

This document has been reviewed and approved per the Review and Approval of Clinical Documents Standard Operating Procedures. Signatures indicate that the final version of the Statistical Analysis Plan (SAP) or amended SAP is released for execution.

Approval Signatures

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