PROTOCOL DV0002 AMENDMENT 1

(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 CHRONIC PLAQUE PSORIASIS

PHASE 3

IND Number: 128707

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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
BMI	body mass index
BP	blood pressure
BSA	body surface area
CDMS	clinical data management system
CI	confidence interval
CRO	contract research organization
ECG	electrocardiogram
eCRF	electronic Case Report form
eC-SSRS	electronic Columbia Suicide Severity Rating Scale
FAS	Full Analysis Set(s)
FAS-a	Full Analysis Set for the bimekizumab-AI-1mL
FAS-s	Full Analysis Set for the bimekizumab-SS-1mL
GCP	Good Clinical Practice
ICF	Informed Consent form
ICH	International Council for Harmonisation
IFU	instructions for use
IGA	Investigator's Global Assessment
IL	interleukin
IMP	investigational medicinal product
IRB	Institutional Review Board
IRT	interactive response technology
PASI	Psoriasis Area Severity Index
PFS	prefilled syringe
PHQ-9	Patient Health Questionnaire 9
PK	pharmacokinetic(s)

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PKS	Pharmacokinetic Set
PKS-PPS-a	Pharmacokinetic Set for the bimekizumab-AI-1mL
PKS-PPS-s	Pharmacokinetic Set for the bimekizumab-SS-1mL
PS	Patient Safety
PSO	psoriasis
Q4W	every 4 weeks
Q8W	every 8 weeks
RNS	rigid needle shield
SADE	serious adverse device effect
SAE	serious adverse event
SAP	Statistical Analysis Plan
sc	subcutaneous
SFU	safety follow-up
SIAQ	Self-injection Assessment Questionnaire
SOP	Standard Operating Procedure
SS	Safety Set(s)
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
TB	tuberculosis
USADE	unanticipated serious adverse device effect
VAS	visual analog scale

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1 SUMMARY

DV0002 is a multicenter, open-label, randomized substudy in adult subjects with moderate to severe chronic plaque psoriasis (PSO) to evaluate the safe and effective use of 4 single-use disposable self-injection investigational devices for the subcutaneous (sc) administration of bimekizumab solution (the investigational medicinal product [IMP]). The 4 self-injection devices to be tested are the 1mL bimekizumab safety syringe (bimekizumab-SS-1mL), the 1mL bimekizumab auto injector (bimekizumab-AI-1mL), the 2mL bimekizumab safety syringe (bimekizumab-SS-2mL), and the 2mL bimekizumab auto injector (bimekizumab-AI-2mL).

DV0002 is a substudy of PS0014, which is a multicenter, open-label, long-term safety study for subjects with moderate to severe chronic plaque PSO who complete 1 of the Phase 3 feeder studies (PS0008, PS0009, or PS0013). The PS0014 study will evaluate the long-term safety, tolerability, and efficacy of bimekizumab in subjects with PSO, and study personnel qualified in sc injection technique will administer bimekizumab to subjects in a 1mL True North prefilled syringe (referred to throughout this protocol as the 1mL PFS). In the DV0002 substudy, subjects will self-administer bimekizumab at DV0002 Baseline and at DV0002 Week 8.

During the Treatment Period of DV0002, subjects will receive either bimekizumab 320mg every 8 weeks (Q8W) or bimekizumab 320mg every 4 weeks (Q4W), based on their assigned dosing at Baseline of PS0014. The same interactive response technology (IRT) will be used for both studies (DV0002 and PS0014). The dose regimen will remain stable for the entire Treatment Period of DV0002.

In the DV0002 substudy, subjects will be assigned to 1 of the 4 self-injection devices and will self-administer bimekizumab only at DV0002 Baseline and at DV0002 Week 8 after training, regardless of their assigned dosing regimen. Bimekizumab will be administered by study personnel at DV0002 Week 4 and DV0002 Week 12 for subjects in the Q4W dosing arm and at DV0002 Week 16 for both dosing arms. A safety follow-up (SFU) telephone call will occur 1 week after the last self-administration (at DV0002 Week 9). After Week 16 in the DV0002 substudy, subjects will continue in PS0014.

The primary objective of the DV0002 substudy 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. The primary 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 bimekizumab-AI-2mL device 8 weeks after training in self-injection technique (DV0002 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 device, which shows that the 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 ADEs [SADEs] and/or ADEs leading to withdrawal from the DV0002 substudy)

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The secondary study objectives and other study objectives are provided in Section 3.2 and Section 3.3, respectively. Of note, one of the other study objectives is to assess trough pharmacokinetic (PK) levels associated with self-injection using the investigational device, injection by study personnel, injection site (abdomen or thigh), and body mass index (BMI) category (by tertile). The secondary outcome variable, other outcome variables, and the other safety variable are listed in Section 4.1.2, Section 4.1.3.1, and Section 4.1.3.3, respectively.

The DV0002 substudy consists of 2 cohorts. The 1mL device cohort will evaluate 2 different self-injection investigational devices: the bimekizumab-SS-1mL and the bimekizumab-AI-1mL. The 2mL device cohort will also evaluate 2 different self-injection investigational devices: the bimekizumab-SS-2mL and the bimekizumab-AI-2ml. The data for each cohort will be analyzed and reported separately.

1mL Device Cohort

Subjects who enroll in the 1mL device cohort of DV0002 will begin the DV0002 substudy and the PS0014 study at the same time, and as such, the Baseline visit and all subsequent study visits (up to Week 16) will be the same.

To compensate for subjects who have different study treatments between the feeder studies and DV0002, the 1mL device cohort of the DV0002 substudy is planned to enroll approximately 200 subjects (100 subjects per device arm) to ensure that approximately 50 subjects per device arm are evaluable for steady state trough PK level analyses. 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.

In the DV0002 substudy 1mL device cohort, 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 by study personnel for safety and effectiveness 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.

2mL Device Cohort

Subjects who participated in the 1mL device cohort are not eligible to participate in the 2mL device cohort. 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 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.

In the DV0002 substudy, for the 2ml devices, the 320mg bimekizumab dose will be self-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.

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2 INTRODUCTION

Psoriasis is a common, chronic inflammatory disease characterized by a series of linked cellular changes in the skin. Bimekizumab (UCB4940; the IMP) is an engineered, humanized full length monoclonal antibody of immunoglobulin G1 subclass that selectively and potently inhibits the activity of interleukin (IL)-17A and IL-17F in vitro. Interleukin-17A and IL-17F are key proinflammatory cytokines believed to play important roles in autoimmune and inflammatory diseases. Bimekizumab is being developed for the treatment of patients with inflammatory diseases such as psoriatic arthritis, PSO, and axial spondyloarthritis.

It is important for patients who may use bimekizumab for the treatment of moderate to severe chronic plaque PSO to have options for the self-injection of bimekizumab that fit their needs and preferences. Whilst some patients may prefer to manually regulate various tasks comprising the self-injection process (eg, needle visibility, skin penetration by needle, speed of self-injection), others may prefer a more automated process (eg, do not wish to see the needle, desire an automatic injection). UCB therefore intends to provide patients with different options to self-inject bimekizumab.

The DV0002 study is a substudy of the PS0014 study. 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 in a 1mL PFS. The DV0002 substudy will evaluate 4 self-injection investigational devices: the bimekizumab-SS-1mL, the bimekizumab-AI-1mL, the bimekizumab-SS-2mL, and the bimekizumab-AI-2ml. Full descriptions of the 4 devices are provided in Section 7.1.1, Section 7.1.2, Section 7.1.3 and Section 7.1.4, respectively.

The proposed substudy is planned to demonstrate that adult subjects with moderate to severe chronic plaque PSO can safely and effectively self-inject bimekizumab using the bimekizumab-SS-1mL, bimikizumab-AI-1mL, bimekizumab-SS-2mL, or bimekizumab-AI-2mL device.

For subjects in the 1mL device cohort, 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. Subjects who participated in the 1mL device cohort of DV0002 are not eligible to enroll in the 2mL device cohort.

Once the 1mL device cohort has finished enrolling, the 2mL device cohort will start enrolling. Subjects in this cohort will be randomly assigned in a 1:1 ratio to perform self-injection using either the bimekizumab-SS-2mL or bimekizumab-AI-2mL device.

3 STUDY OBJECTIVES

3.1 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.

3.2 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 self-injection technique using the devices.

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3.3 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 PK (trough bimekizumab) levels associated with self-injection using the investigational devices, injection by study personnel, injection site (abdomen or thigh), and 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.

4 STUDY VARIABLES

4.1 Outcome variables

4.1.1 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, bimekizumab-AI-1mL, 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 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.

4.1.2 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

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be evaluated by study personnel and is defined as for the primary outcome variable (see Section 4.1.1).

4.1.3 Other variables

4.1.3.1 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 (see Section 9.1).
- 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 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.

4.1.3.2 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.

4.1.3.3 Safety variable

The other safety variable is the occurrence of ADEs. Additional safety and tolerability variables will be collected as described in the PS0014 study protocol.

5 STUDY DESIGN

5.1 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, and 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 solution 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 instructions for use (IFU) and any other applicable training materials.

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1mL Device Cohort

For the 1mL device cohort, 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).

During the 16-week Treatment Period of DV0002, subjects will receive either bimekizumab 320mg Q8W or bimekizumab 320mg Q4W, based on their assigned dosing at Baseline (Table 5-1). Baseline for DV0002 and Baseline for PS0014 will occur at the same time, and the same interactive response technology (IRT) will be used for both studies. The 320mg bimekizumab dose will be administered as two 160mg injections, and both injections will be either self-administered using the investigational device (at Baseline and Week 8) or administered by study personnel using the 1mL PFS (at Week 4 and Week 12 for subjects in the Q4W dosing arm and at Week 16 for both dosing arms). This dose regimen will remain stable for the entire 16-week Treatment Period of DV0002, as per PS0014 design. The DV0002 substudy will evaluate 2 self-injection investigational devices: the bimekizumab-SS-1mL and the bimekizumab-AI-1mL.

Eligible subjects (PS0014 entry criteria and Section 6 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 (see Section 7.10). 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).

Table 5-1: Bimekizumab administration schedule visits in DV0002 substudy 1mL device cohort

Dose Regimen	Baseline	Week 4	Week 8	Week 12	Week 16
320mg Q8W	S	NA	S	NA	SP
320mg Q4W	S	SP	S	SP	SP

bimekizumab-AI-1mL=1mL bimekizumab auto-injector; bimekizumab-SS-1mL=1mL bimekizumab safety syringe; NA=not applicable; Q4W=every 4 weeks; Q8W=every 8 weeks; S=subject performing self-injection using the investigational device; SP=study personnel performing injection using the 1mL pre-filled syringe

Note: For S injections, the 320mg bimekizumab dose will be administered as two 160mg injections (using 2 bimekizumab-SS-1mL or 2 bimekizumab-AI-1mL). For SP injections, the 320mg bimekizumab dose will be administered as two 160mg injections (using prefilled syringes). Both injections will be administered in the same manner (eg, both self-administered injections or both study personnel-administered injections), but each injection will be administered at a separate injection site and rotation between injection sites should be observed.

Note: For the 1mL device cohort, visits in the DV0002 substudy correlate with the same visit in the PS0014 study (ie, the DV0002 Baseline Visit is the PS0014 Baseline Visit). Dose regimen will be assigned at Baseline, and the same interactive response technology will be used for both studies.

The bimekizumab administration schedule optimizes the collection of PK trough level data within the constraints of a short treatment period and a Q4W and Q8W dosing regimen. At Weeks 4, 12, and 16, subjects on the Q4W dosing regimen will be injected by study personnel with 2 injections each of 160mg bimekizumab using a 1mL PFS (ie, the same device as that used

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in PS0014). For these subjects, the Q4W administration schedule will provide PK trough data associated with injection by:

- *Study personnel using the 1mL PFS* from PK samples collected (before self-injection) at Baseline and Week 8 (ie, PK data from 2 timepoints)
- *Subject self-injection using the assigned device* from PK samples collected (before injection by study personnel) at Week 4 and Week 12 (ie, PK data from 2 timepoints)

At Baseline and Week 8, subjects on the Q8W dosing regimen will self-inject 2 injections each of 160 mg bimekizumab using the assigned device (ie, bimekizumab-SS-1mL or the bimekizumab-AI-1mL). For these subjects, the Q8W administration schedule will provide PK trough data associated with injection by:

- *Study personnel using the 1mL PFS* from PK samples collected (before self-injection) at Baseline (ie, PK data from 1 timepoint)
- *Subject self-injection using the assigned device* from PK samples collected (before self-injection) at Week 8 and (before injection by study personnel) at Week 16 (ie, PK data from two timepoints)

In addition to self-injections, DV0002 substudy-specific assessments (eg, study personnel evaluation, SIAQ responses, VAS for injection site pain, and PK analyses; see Section 5.2) will be performed from Baseline through Week 16 (inclusive). An SFU telephone call will occur 1 week after the last self-administration (at Week 9).

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). Studies DV0002 and PS0014 will share a common database/electronic Case Report form (eCRF) system (including common adverse event [AE] reporting) and a common IRT.

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 (see Section 6.3). Subjects who are withdrawn from bimekizumab treatment (PS0014 study) during the course of DV0002 will also be required to follow the PS0014 withdrawal procedures.

2mL Device Cohort

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.

During the Treatment Period of DV0002, subjects will receive either bimekizumab 320mg Q8W or bimekizumab 320mg Q4W, based on their assigned dosing at Baseline of PS0014 (Table 5-3). 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. The same IRT will be used for both studies. The 320mg bimekizumab dose will either be self-administered as 1 injection using the assigned

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investigational device (at DV0002 Baseline and Week 8) or administered as 2 injections by study personnel using the 1mL PFS (at DV0002 Week 4 and Week 12 for subjects in the Q4W dosing arm and at DV0002 Week 16 for both dosing arms). This dose regimen will remain stable for the entire 16-week Treatment Period of DV0002, per the PS0014 design.

Eligible subjects (PS0014 entry criteria and Section 6 DV0002 entry criteria) who have not participated in the 1mL device cohort, will be randomly assigned in a 1:1 ratio to perform self-injection using either the bimekizumab-SS-2mL or the bimekizumab-AI-2mL (see Section 7.10). Regardless of the assigned dose regimen, subjects will perform self-injection with the assigned devices only at DV0002 Baseline and at DV0002 Week 8.

Table 5-2: Bimekizumab administration schedule visits in DV0002 substudy 2mL device cohort

	DV0002 Visits				
Dose Regimen	**Baseline**	**Week 4**	**Week 8**	**Week 12**	**Week 16**
320mg Q8W	S	NA	S	NA	SP
320mg Q4W	S	SP	S	SP	SP

bimekizumab-AI-2mL=2mL bimekizumab auto-injector; bimekizumab-SS-2mL=2mL bimekizumab safety syringe; IRT = interactive response technology; NA=not applicable; Q4W=every 4 weeks; Q8W=every 8 weeks; S=subject performing self-injection using the investigational device; SP=study personnel performing injection using the 1mL prefilled syringe

Note: For S injections, the 320mg bimekizumab dose will be administered as a single injection (using the bimekizumab-SS-2mL or bimekizumab-AI-2mL devices). For SP injections, the 320mg bimekizumab dose will be administered as two 160mg injections (using 2 prefilled syringes). The injections will be administered in the same manner (eg, both self-administered injections or both SP-administered injections), but each injection will be administered at a separate injection site and rotation between injection sites should be observed.

Note: For the 2mL device cohort, Baseline for DV0002 will occur at PS0014 Week 24, Week 28, or Week 32 for subjects receiving bimekizumab Q4W or at PS0014 Week 24 or Week 32 for subjects receiving bimekizumab Q8W. Dose regimen will be assigned at Baseline of the PS0014 study, and the same IRT will be used for both the PS0014 and DV0002 studies.

The bimekizumab administration schedule optimizes the collection of PK trough data within the constraints of a short treatment period and a Q4W and Q8W dosing regimen. At Weeks 4, 12, and 16, subjects on the Q4W dosing regimen will be injected by study personnel with 2 injections each of 160 mg bimekizumab using a 1mL PFS (ie, the same device as that used in PS0014). For these subjects, the Q4W administration schedule will provide PK trough data associated with injection by:

- *Study personnel using the 1mL PFS* from PK samples collected (before self-injection) at DV0002 Baseline and Week 8 (ie, PK data from 2 timepoints)
- *Subject self-injection using the assigned device* from PK samples collected (before injection by study personnel) at Week 4 and Week 12 (ie, PK data from 2 timepoints)

At DV0002 Baseline and Week 8, subjects on the Q8W dosing regimen will self-inject 1 injection using the assigned 2mL device (bimekizumab-SS-2mL or the 1 bimekizumab-AI-2mL).

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For these subjects, the Q8W administration schedule will provide PK trough data associated with injection by:

- *Study personnel using the 1mL PFS* from PK samples collected (before self-injection) at DV0002 Baseline (ie, PK data from 1 timepoint)
- *Subject self-injection using the assigned device* from PK samples collected (before self-injection) at DV0002 Week 8 and (before injection by study personnel) at DV0002 Week 16 (ie, PK data from 2 timepoints)

In addition to self-injections, DV0002 substudy-specific assessments (eg, study personnel evaluation, SIAQ responses, VAS for injection site pain, and PK analyses; see Section 5.2) will be performed from DV0002 Baseline through Week 16 (inclusive). An SFU telephone call will occur 1 week after the last self-administration (at DV0002 Week 9).

After Week 16 in the DV0002 substudy, subjects will continue in PS0014. Studies DV0002 and PS0014 will share a common database/eCRF system (including common AE reporting) and a common IRT.

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 (see Section 6.3). Subjects who are withdrawn from bimekizumab treatment (PS0014 study) during the course of DV0002 will also be required to follow the PS0014 withdrawal procedures.

5.1.1 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 Week 16 Visit or withdraws from the study.

5.1.2 Planned number of subjects and sites

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.

5.1.3 Anticipated regions and countries

This substudy will be conducted in North America.

5.2 Schedule of study assessments

The schedule of assessments in presented in Table 5-3 for the 1mL device cohort. For subjects in the 1mL device cohort, Baseline for DV0002 corresponds to Baseline in PS0014, and the subsequent study visits are the same in both studies. Table 5-3 includes assessments performed specifically in the DV0002 substudy and assessments performed as part of the PS0014 study, inclusive. Assessments specific to the DV0002 substudy are labeled for clarity.

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For subjects in the 2mL device cohort, Baseline for DV0002 can correspond to the PS0014 Week 24, Week 28, or Week 32 visits for subjects receiving bimekizumab Q4W and to the PS0014 Week 24 or Week 32 visits for subjects receiving bimekizumab Q8W. The schedule of assessments for the PS0014 Week 24 through Week 48 visits is presented in Table 5-4. The additional assessments to be performed for the DV0002 substudy in the 2mL device cohort specifically are presented in Table 5-5.

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Table 5-3: Schedule of assessments for the PS0014 study and DV0002 substudy (1mL device cohort)

Procedures / Visit [a] Week	DV0002 Treatment Period					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (DV0002 SFU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16
Informed consent for DV0002 and PS0014 assessments	X					
Inclusion/exclusion	X					
Physical exam [b, c]	X				X	
Body weight	X					
Vital signs [d]	X	X	X			X
Hematology and chemistry	X	X	X			X
Urinalysis	X	X	X			X
Urine drug screen	X					
ECG	X					
Pregnancy testing [e]	X	X	X		X	X
TB questionnaire	X				X	
Blood sample for bimekizumab plasma concentrations [f] (DV0002-specific for Weeks 4, 8, and 12)	X	X [g]	X		X [g]	X [h]
Blood sample for anti-bimekizumab antibodies [f]	X					X
PASI	X	X	X		X	X
Percentage of BSA	X	X	X		X	X

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Table 5-3: Schedule of assessments for the PS0014 study and DV0002 substudy (1mL device cohort)

Procedures / Visit [a] Week	DV0002 Treatment Period					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (DV0002 SFU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16
IGA	X	X	X		X	X
DLQI	X					
PHQ-9	X	X	X			X
eC-SSRS	X	X	X			X
mNAPSI [i]	X					
Scalp IGA [j]	X					
pp-IGA [k]	X					
EQ-5D-3L	X					
SF-36	X					
PGA of PSO	X					
PASE	X					
PGADA [l]	X					
WPAI-SHP v2.0	X					
Concomitant medication (DV0002-specific for Week 9)	X	X	X	X	X	X
Adverse events [m] (DV0002-specific for Week 9)	X	X	X	X	X	X

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Table 5-3: Schedule of assessments for the PS0014 study and DV0002 substudy (1mL device cohort)

Procedures / Visit [a] Week	DV0002 Treatment Period					
	Visit 1	**Visit 2**	**Visit 3**	**Visit 3a Telephone Call (DV0002 SFU)**	**Visit 4**	**Visit 5**
	Baseline/Feeder Study Final Visit	**Week 4**	**Week 8**	**Week 9**	**Week 12**	**Week 16**
Random assignment to device (DV0002-specific)	X					
IRT contact	X	X	X		X	X
Subject training for VAS and SIAQ Questionnaire (DV0002-specific)	X					
Pre-injection SIAQ Questionnaire [n] (DV0002-specific)	X					
Subject training for self-injection (DV0002-specific)	X					
Bimekizumab administration by study personnel using the PFS [o]		X [g]			X [g]	X
Subject self-injection of bimekizumab using the assigned device [o, p] (DV0002-specific)	X		X			
Study personnel evaluation of self-injection (DV0002-specific)	X		X			
Study personnel evaluation of post-use device for structural/mechanical integrity (DV0002-specific)	X		X			

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Table 5-3: Schedule of assessments for the PS0014 study and DV0002 substudy (1mL device cohort)

Procedures \ Visit [a] Week	DV0002 Treatment Period					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (DV0002 SFU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16
VAS for injection site pain (DV0002-specific)	X		X			
Post-injection SIAQ Questionnaire [n] (DV0002-specific)	X		X			
Drug and device accountability (DV0002-specific)	X	X[g]	X		X[g]	X

bimekizumab-AI-1mL=1mL bimekizumab auto-injector; bimekizumab-SS-1mL=1mL bimekizumab safety syringe; BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; PASI=Psoriasis Area Severity Index; PGA=Patient Global Assessment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire 9; pp-IGA=palmoplantar Investigator's Global Assessment; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; SF-36=Short Form 36-item Health Survey; SFU=safety follow-up; SIAQ=Self-injection Assessment Questionnaire; TB=tuberculosis; VAS=visual analog scale; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

[a] Visit windows of ±7 days from the first dose at all visits except Visit 3a (SFU telephone call). The SFU telephone call window is 7 days from the last dose in the DV0002 substudy, ±3 days.

[b] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.

[c] The physical exam will include examination of the following systems: eyes, hair, and skin; respiratory; cardiovascular; and gastrointestinal.

[d] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.

[e] Pregnancy testing will consist of urine pregnancy tests at all visits. Pregnancy test results must be negative prior to administering investigational medicinal product.

[f] All blood samples will be taken prior to dosing.

[g] This will only be done for subjects who receive bimekizumab Q4W.

[h] This will only be done for subjects who receive bimekizumab Q8W.

[i] The mNAPSI will be assessed only in subjects with nail involvement at Baseline in the feeder studies.

[j] The scalp IGA will only be assessed for those subjects with scalp involvement (scalp IGA score >0) at Baseline in the feeder studies.

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Table 5-3: Schedule of assessments for the PS0014 study and DV0002 substudy (1mL device cohort)

Procedures \ Visit [a] Week	DV0002 Treatment Period					
	Visit 1	**Visit 2**	**Visit 3**	**Visit 3a Telephone Call (DV0002 SFU)**	**Visit 4**	**Visit 5**
	Baseline/Feeder Study Final Visit	**Week 4**	**Week 8**	**Week 9**	**Week 12**	**Week 16**

[k] The pp-IGA will only be assessed in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline in the feeder studies.
[l] The PGADA is assessed only for subjects with psoriatic arthritis at Baseline in the feeder studies.
[m] Adverse events not related to the investigational devices will be reported in PS0014 and adverse device effects and device deficiencies will be reported in DV0002. A single safety database will be used for both studies.
[n] Version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL, while version 2.1 will be used to assess bimekizumab-AI-1mL (see Section 9.1).
[o] The dosing window is ±7 days relative to the scheduled dosing visit.
[p] The 320mg bimekizumab dose will be administered as two 160mg injections (using 2 bimekizumab-SS-1mL devices or 2 bimekizumab-AI-1mL devices).

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Table 5-4: Schedule of assessments for the PS0014 study (2mL device cohort)

Procedures \ Week	Week 24[a]	Week 28[a]	Week 32[a]	Week 36	Week 40	Week 44	Week 48
Physical exam[b,c]	X			X			X
Body weight							X
Vital signs[d]	X		X		X		X
Hematology and chemistry	X		X		X		X
Urinalysis	X		X		X		X
ECG							X
Pregnancy testing[e]	X	X	X	X	X	X	X
IGRA TB test							X
TB questionnaire	X			X			X
Blood sample for bimekizumab plasma concentrations[f]	X				X		X
Blood sample for anti-bimekizumab antibodies[f]	X				X		X
PASI	X	X	X	X	X	X	X
Percentage of BSA	X	X	X	X	X	X	X
IGA	X	X	X	X	X	X	X
DLQI	X						X
PHQ-9	X		X		X		X
eC-SSRS	X		X		X		X
mNAPSI[g]	X						X
Scalp IGA[h]	X						X

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Table 5-4: Schedule of assessments for the PS0014 study (2mL device cohort)

Week / Procedures	Week 24[a]	Week 28[a]	Week 32[a]	Week 36	Week 40	Week 44	Week 48
pp-IGA[i]	X						X
EQ-5D-3L	X						X
SF-36	X						X
PGA of PSO	X						X
PASE[j]							X
PGADA[j]	X						X
WPAI-SHP V2.0	X						X
TSQM-9							X
Concomitant medication	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X
IRT	X	X	X	X	X	X	X
Bimekizumab administration[k,l]	X	X	X	X	X	X	X
Subject training on home self-injection[m]					X	X	

BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; PASI=Psoriasis Area Severity Index; PGA=Patient Global Assessment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire-9; pp-IGA=palmoplantar Investigator's Global Assessment; PsA=psoriatic arthritis; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; SF-36=Short Form 36-item Health Survey; TB=tuberculosis; TSQM-9=Treatment Satisfaction Questionnaire for Medication; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

Note: Starting at Week 48 of the PS0014 Treatment Period, subjects may self-inject IMP at home; self-injection training will be provided to the subject/caregivers by qualified site personnel (refer to PS0014 protocol).

[a] For the 2mL device cohort, Baseline of DV0002 can occur at PS0014 Week 24, Week 28, or Week 32 for subjects receiving bimekizumab Q4W and at PS0014 Week 24 or Week 32 for subjects receiving bimekizumab Q8W.

[b] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.

[c] The physical examination will be performed as per the PS0014 protocol Section 9.3.5.

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Table 5-4: Schedule of assessments for the PS0014 study (2mL device cohort)

Procedures \ Week	Week 24[a]	Week 28[a]	Week 32[a]	Week 36	Week 40	Week 44	Week 48

[d] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.
[e] Urine pregnancy testing will be performed at all visits. Pregnancy test results must be negative prior to administering IMP.
[f] All blood samples taken prior to dosing.
[g] The mNAPSI will be assessed only in subjects with nail involvement at Baseline in the feeder studies.
[h] The scalp IGA will only be assessed for those subjects with scalp involvement (scalp IGA score >0) at Baseline in the feeder studies.
[i] The pp-IGA will only be assessed in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline in the feeder studies
[j] The PGADA and the PASE are assessed only for subjects with PsA at Baseline in the feeder studies.
[k] The dosing window is ±7 days relative to the scheduled dosing visit.
[l] Only subjects receiving IMP Q4W are dosed on Week 28, Week 36, and Week 44.
[m] Subject training on at-home self-injection is to be performed as described in the PS0014 protocol Section 7.2. Starting at Week 48 of the PS0014 Treatment Period, subjects may self-inject IMP at home.

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Table 5-5: Schedule of assessments for the DV0002 substudy (2mL device cohort)

Visit[a] / Week / Procedures	DV0002 Treatment Period					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (Device SFU)	Visit 4	Visit 5
	Baseline[b]	Baseline + 4 weeks	Baseline + 8 weeks	Baseline + 9 weeks	Baseline + 12 weeks	Baseline + 16 weeks
Informed consent for DV0002	X					
Random assignment to device (DV0002-specific)	X					
IRT contact	X	X	X		X	X
Blood sample for bimekizumab plasma concentrations[c] (DV0002-specific for Weeks 4, 8, and 12)	X	X[d]	X		X[d]	X[e]
Subject training for VAS and SIAQ Questionnaire (DV0002-specific)	X					
Pre-injection SIAQ Questionnaire[f] (DV0002-specific)	X					
Subject training for self-injection (DV0002-specific)	X					
Bimekizumab administration by study personnel using the PFS[g]		X[d]			X[d]	X
Subject self-injection of bimekizumab using the assigned device[g,h] (DV0002-specific)	X		X			
Study personnel evaluation of self-injection (DV0002-specific)	X		X			

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Table 5-5: Schedule of assessments for the DV0002 substudy (2mL device cohort)

Visit[a] / Week / Procedures	DV0002 Treatment Period					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (Device SFU)	Visit 4	Visit 5
	Baseline[b]	Baseline + 4 weeks	Baseline + 8 weeks	Baseline + 9 weeks	Baseline + 12 weeks	Baseline + 16 weeks
VAS for injection site pain (DV0002-specific)	X		X			
Post-injection SIAQ Questionnaire[f] (DV0002-specific)	X		X			
Study personnel evaluation of post-use device for structural/mechanical integrity (DV0002-specific)	X		X			
Drug and device accountability (DV0002-specific)	X	X[d]	X		X[d]	X
Concomitant medication				X		
Adverse Events[i]				X		

IRT=interactive response technology; Q4W=every 4 weeks; Q8W=every 8 weeks; SFU=safety follow-up; SIAQ=Self-injection Assessment Questionnaire; VAS=visual analog scale

[a] Visit windows of ±7 days from the first dose at all visits except Visit 3a (SFU telephone call). The SFU telephone call window is 7 days from the last dose in the DV0002 substudy, ±3 days.

[b] For subjects in the 2mL device cohort, Baseline for DV0002 corresponds to PS0014 Week 24, Week 28, or Week 32 for subjects receiving bimekizumab Q4W and to PS0014 Week 24 or Week 32 for subjects receiving bimekizumab Q8W. Refer to Table 5-4 for PS0014 study assessments.

[c] All blood samples will be taken prior to dosing. For detail on PK sampling in the 2mL device cohort, refer to Table 10-1 in Section 10.

[d] This will only be done for subjects who receive bimekizumab Q4W.

[e] This will only be done for subjects who receive bimekizumab Q8W.

[f] Version 2.0 of the SIAQ will be used to assess bimekizumab-SS-2mL, while version 2.1 will be used to assess bimekizumab-AI-2mL (see Section 9.1).

[g] The dosing window is ±7 days relative to the scheduled dosing visit.

[h] The 320mg bimekizumab dose will be administered as 1 injection using the bimekizumab-SS-2mL device or bimekizumab-AI-2mL device.

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Table 5-5: Schedule of assessments for the DV0002 substudy (2mL device cohort)

Procedures \ Visit[a] Week	DV0002 Treatment Period					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (Device SFU)	Visit 4	Visit 5
	Baseline[b]	Baseline + 4 weeks	Baseline + 8 weeks	Baseline + 9 weeks	Baseline + 12 weeks	Baseline + 16 weeks

[i] Adverse events not related to the devices will be reported in PS0014 and adverse device effects and device deficiencies will be reported in DV0002. A single safety database will be used for both studies.

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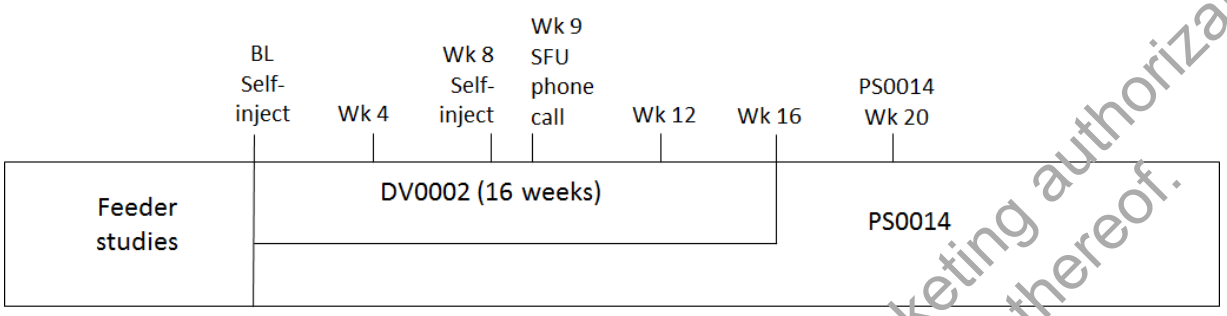
5.3 Schematic diagram

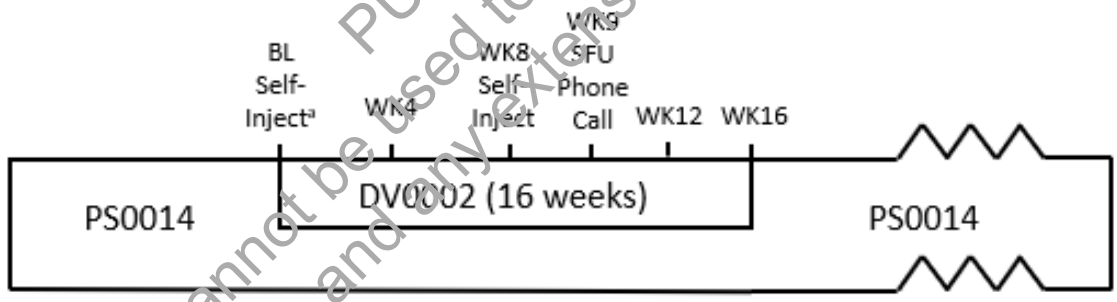
The study schematic diagram for DV0002 1 mL device cohort is presented in Figure 5–1, and the 2mL device cohort is presented in Figure 5–2.

Figure 5–1: Schematic diagram for the 1mL device cohort



BL=Baseline; Q4W=every 4 weeks; Q8W=every 8 weeks; self-inject=self-injection; SFU=safety follow-up; Wk=week
Note: Phase 3 feeder studies include PS0008, PS0009, and PS0013.
Note: Subjects will receive 320mg bimekizumab either Q4W or Q8W. Bimekizumab will be self-administered only at Baseline and at Week 8 (study personnel will administer bimekizumab at other visits, as applicable).
Note: For the 1mL device cohort, subjects will begin the DV0002 substudy and the PS0014 study at the same time; therefore, Baseline for DV0002 corresponds to Baseline for PS0014.

Figure 5–2: Schematic diagram for the 2mL device cohort



BL=Baseline; Q4W=every 4 weeks; Q8W=every 8 weeks; self-inject=self-injection; SFU=safety follow-up; WK=week
Note: Subjects will receive 320mg bimekizumab either Q4W or Q8W. Bimekizumab will be self-administered only at DV0002 Baseline and 8 weeks after training (study personnel will administer bimekizumab at other visits).
[a] For the 2mL device cohort, subjects will not begin the DV0002 substudy and the PS0014 study at the same time. Baseline for DV0002 corresponds to the PS0014 Week 24, Week 28, or Week 32 visit for subjects receiving bimekizumab Q4W and to the PS0014 Week 24 or Week 32 visit for subjects receiving bimekizumab Q8W.

5.4 Rationale for study design and selection of dose

DV0002 is a Phase 3, randomized, multicenter, open-label study for subjects with moderate to severe chronic plaque PSO who will self-inject bimekizumab. DV0002 is a substudy of PS0014; PS0014 is a multicenter, open-label, long-term study to evaluate the safety, tolerability, and

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efficacy of bimekizumab in subjects with moderate to severe chronic plaque PSO who complete 1 of the Phase 3 feeder studies (PS0008, PS0009, or PS0013).

It is expected that most individuals who will use commercial bimekizumab for the treatment of moderate to severe chronic plaque PSO will self-inject bimekizumab and also that these individuals will prefer to have options for the self-administration of their medication. DV0002 will therefore evaluate the safe and effective use of 4 different self-injection investigational devices in 2 cohorts: the 1mL device cohort and the 2mL device cohort. The 1mL device cohort will evaluate the bimekizumab-SS-1mL and bimekizumab-AI-1mL investigational devices. The 2mL device cohort will evaluate the bimekizumab-SS-2mL and bimekizumab-AI-2mL investigational devices. In addition, DV0002 will assess trough PK levels associated with self-injection using the investigational device, injection by study personnel using the 1mL PFS, injection site (abdomen or thigh), and BMI category (by tertile).

6 SELECTION AND WITHDRAWAL OF SUBJECTS

6.1 Inclusion criteria

To be eligible for DV0002, subjects must meet all of the following additional criteria:

1. An Institutional Review Board (IRB) approved written Informed Consent form (ICF) for DV0002 is signed and dated by the subject.
2. Subject fulfills all inclusion criteria for the PS0014 study.
3. Subject is considered reliable and capable of adhering to the DV0002 protocol (eg, able to understand and complete questionnaires, able to use investigational device according to the IFU, and able to adhere to the visit schedule) according to the judgment of the Investigator.
4. Subject is willing to self-inject.

6.2 Exclusion criteria

Subjects are not permitted to enroll in DV0002 if any of the PS0014 study exclusion criteria are met. Subjects who participated in the 1mL device cohort of DV0002 are not eligible to enroll in the 2mL device cohort.

6.3 Withdrawal criteria

Since DV0002 is a substudy of PS0014, all DV0002 withdrawal criteria are captured in the PS0014 protocol. There are no additional DV0002-specific withdrawal criteria beyond those that are described in PS0014. Subjects are free to withdraw from DV0002 at any time, without prejudice to their continued care. Subjects who withdraw from DV0002 but remain eligible for PS0014 (ie, subjects who have a medical condition or personal preference that precludes further self-injection) may continue in PS0014. These subjects must perform an SFU telephone call 1 week after their final DV0002 dosing visit.

Subjects who are withdrawn from bimekizumab treatment (PS0014 study) during DV0002 will also be required to follow the PS0014 withdrawal procedures.

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7 INVESTIGATIONAL MEDICINAL PRODUCT AND INVESTIGATIONAL DEVICE

In the DV0002 substudy, the term IMP refers to the bimekizumab drug product. The term investigational device refers to 4 different self-injection investigational devices (bimekizumab-SS-1mL, bimekizumab-AI-1mL, bimekizumab-SS-2mL, and bimekizumab-AI-2mL) that are comprised of drug product (IMP) associated with a functional secondary packaging.

7.1 Description of investigational devices

At DV0002 Baseline, each subject will be provided with self-injection training and IFU for the appropriate device.

7.1.1 Bimekizumab-SS-1mL

The bimekizumab-SS-1mL, shown in Figure 7-1, consists of the naked PFS (primary packaging containing bimekizumab drug product for all Phase 3 studies) and a customized CCI safety syringe for sc bimekizumab administration.

The naked PFS is a glass, 1mL long, primary container with small round flange and a 27G half-inch staked needle containing 1mL of bimekizumab. The CCI safety syringe is a single-use platform device with a passive needle stick safety mechanism. To enhance the device usability, CCI
CCI

Figure 7-1: Bimekizumab-SS-1mL

bimekizumab-SS-1mL=1mL bimekizumab safety syringe; SnS=Safe'n'Sound

7.1.1.1 Instruction for use of bimekizumab-SS-1mL

The bimekizumab-SS-1mL is used to administer an sc injection in either the right or left lateral abdominal wall or the right or left outer thigh without massage. Each injection should be administered at a separate injection site, and rotation between the injection sites should be

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observed. Treatment of the injection site with an anesthetic cream prior to dosing is not permitted.

During the study (at Baseline and Week 8), 2 bimekizumab-SS-1mL devices will be used to administer 160mg injections of bimekizumab (320mg total). To use the bimekizumab-SS-1mL, the overcap is removed and the plunger rod is fully depressed, which empties the syringe contents through the needle. When the plunger rod reaches its final position the needle safety retraction mechanism is activated, which retracts the sleeve, syringe, and plunger rod and holds the needle safely within the body molding.

Additional instructions for device use, including the injection angle, are provided in the IFU.

7.1.2 Bimekizumab-AI-1mL

The bimekizumab-AI-1mL, shown in Figure 7-2, consists of the naked PFS (primary packaging containing bimekizumab drug product used for all Phase 3 studies and in the bimekizumab-SS-1mL) and a customized auto-injector. The PFS volume will be administered from the same primary container, a 1mL long glass syringe, with a small round flange and a 27G half-inch stacked needle. The bimekizumab-AI-1mL is a single dose, disposable, nonsterile combination product. To enhance the device usability, UCB customized the auto-injector by adding a ring-pull cap and an external envelope.

Figure 7-2: Bimekizumab-AI-1mL

bimekizumab-AI-1mL=1mL bimekizumab auto-injector

7.1.2.1 Instruction for use of bimekizumab-AI-1mL

The bimekizumab-AI-1mL is used to administer an sc injection in either the right or left lateral abdominal wall or the right or left outer thigh without massage. Each injection should be administered at a separate injection site, and rotation between the injection sites should be observed. Treatment of the injection site with an anesthetic cream prior to dosing is not permitted.

During the study (at Baseline and Week 8), 2 bimekizumab-AI-1mL devices will be used to administer 160mg injections of bimekizumab (320mg total). To use the bimekizumab-AI-1mL, the ring-pull cap is removed and the device is depressed on the injection site. The auto-injector provides needle insertion, dose delivery, and needle protection through an extending and locking

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shroud. Needle protection is performed by a shroud that will deploy should the auto-injector lose contact with the skin during an injection.

Additional instructions for device use, including the injection angle, are provided in the IFU.

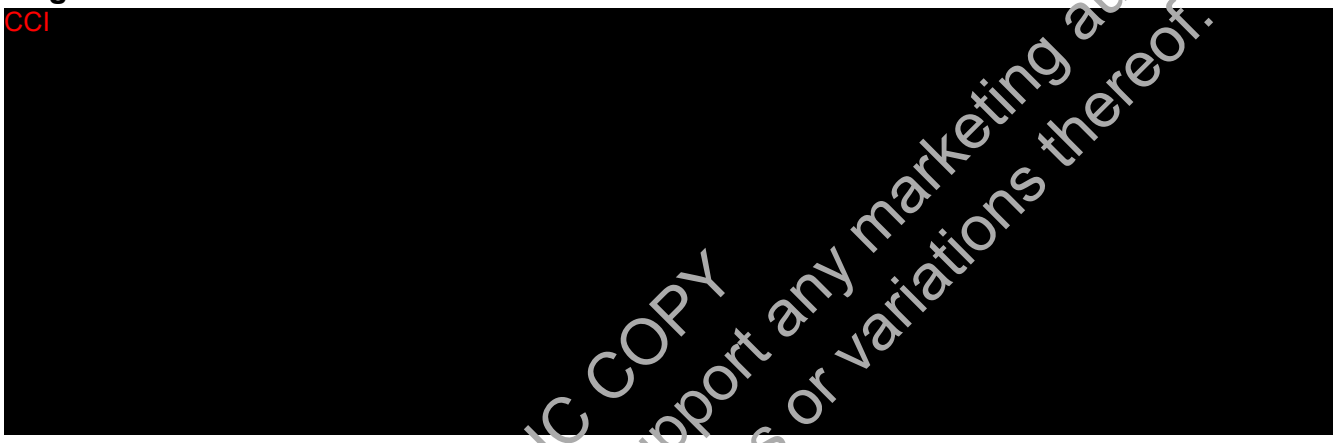
7.1.3 Bimekizumab-SS-2mL

The bimekizumab-SS-2mL, shown in Figure 7-3, consists of the primary container (a glass syringe filled with 2mL of bimekizumab drug product) and a safety syringe.

The bimekizumab-SS-2mL is a single-use syringe with a passive safety feature.

Figure 7-3: Bimekizumab-SS-2mL

CCI



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7.1.3.1 Instruction for use of bimekizumab-SS-2mL

The bimekizumab-SS-2mL is used to administer a sc injection in either the right or left lateral abdominal wall or the right or left outer thigh without massage. Treatment of the injection site with an anesthetic cream prior to dosing is not permitted.

During the study (at DV0002 Baseline and Week 8), 1 bimekizumab-SS-2mL device will be used to administer a 320mg injection of bimekizumab. To use the bimekizumab-SS-2mL, the rigid needle shield (RNS) is removed, and the plunger rod is fully depressed, which empties the syringe contents through the needle. When the plunger rod reaches its final position the needle safety retraction mechanism is activated, which retracts the sleeve, syringe, and plunger rod and holds the needle safely within the body molding.

Additional instructions for device use, including the injection angle, are provided in the IFU.

7.1.4 Bimekizumab-AI-2mL

The bimekizumab-AI-2mL, shown in Figure 7-4, consists of the primary container (a glass syringe filled with 2mL of bimekizumab drug product) and an auto injector. The bimekizumab-AI-2mL is a single use auto injector with a passive needle stick safety mechanism.

Figure 7-4: Bimekizumab-AI-2mL

bimekizumab-AI-2mL=2mL bimekizumab auto-injector

7.1.4.1 Instruction for use of bimekizumab-AI-2mL

The bimekizumab-AI-2mL is used to administer a sc injection in either the right or left lateral abdominal wall or the right or left outer thigh without massage. Treatment of the injection site with an anesthetic cream prior to dosing is not permitted.

During the study (at DV0002 Baseline and Week 8), 1 bimekizumab-AI-2mL device will be used to administer a 320mg injection of bimekizumab. To use the bimekizumab-AI-2mL, the cap is removed, and the device is depressed on the injection site. The auto injector provides needle insertion, dose delivery, and needle protection through an extending and locking shroud. Needle protection is performed by a shroud that will deploy should the auto-injector lose contact with the skin during an injection.

Additional instructions for device use, including the injection angle, are provided in the IFU.

7.2 Treatment to be administered

The IMP used in this study is bimekizumab. Bimekizumab will be supplied at a concentration of 160mg/mL (55mM sodium acetate, 220mM glycine, 0.04% polysorbate 80 at pH 5.0) for sc injection.

1mL Device Cohort

For the 1mL device cohort, IMP will be supplied in 2 investigational devices: bimekizumab-SS-1mL or the bimekizumab-AI-1mL.

The IMP will be administered according to the schedule shown in Table 5-1. Subjects will be assigned to the use of 1 device and will receive the following doses of IMP based on their established dosing regimen in PS0014:

- 320mg bimekizumab, Q8W or

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- 320mg bimekizumab, Q4W.

Regardless of the assigned dose regimen, subjects will perform self-injection with the assigned device only at Baseline and at Week 8. For the 1mL device cohort, the 320mg bimekizumab dose will be administered as two 160mg injections with either 2 bimekizumab-SS-1mL or 2 bimekizumab-AI-1mL devices. At all visits except Baseline and Week 8, the 320mg bimekizumab dose will be administered as two 160mg injections in a 1mL PFS by study personnel (ie, the same administration manner and device used in PS0014).

The investigational devices will be used as described in the IFU. Subjects will be observed onsite for 30 minutes after self-injection with bimekizumab for any AEs. Subjects will be asked to contact the designated site personnel in case any AEs occur outside of the site visits. Of note, reported AEs related to IMP will be assessed within PS0014 and reported ADEs and device deficiencies will be assessed within DV0002.

2mL Device Cohort

For the 2mL device Cohort, IMP will be supplied in 2 investigational devices: bimekizumab-SS-2mL or bimekizumab-AI-2mL.

The IMP will be administered according to the schedule shown in Table 5-2. Subjects will be assigned to the use of 1 device and will receive the following doses of IMP based on their dosing regimen in PS0014:

- 320mg bimekizumab, Q8W or
- 320mg bimekizumab, Q4W.

Regardless of the assigned dose regimen, subjects will perform self-injection with the assigned device only at DV0002 Baseline and 8 weeks after training with the investigational device. For the 2mL device cohort, 320mg bimekizumab dose will be administered as 1 injection with either the bimekizumab-SS-2mL device or the bimekizumab-AI-2mL device. For subjects who receive bimekizumab Q4W, the bimekizumab dose at Week 4 will be administered as two 160mg injections in a 1mL PFS by study personnel (ie, the same administration manner used in PS0014).

The devices will be used as described in the IFU. Subjects will be observed onsite for 30 minutes after self-injection with bimekizumab for any AEs. Subjects will be asked to contact the designated site personnel in case any AEs occur outside of the site visits. Of note, reported AEs related to IMP will be assessed within PS0014 and reported ADEs and device deficiencies will be assessed within DV0002.

7.3 Packaging

The site will receive uniquely-numbered investigational devices (bimekizumab-SS-1mL, bimekizumab-AI-1mL, bimekizumab-SS-2mL, and bimekizumab-AI-2mL) for use in the DV0002 substudy.

7.4 Labeling

Clinical drug and investigational device supplies will be labeled in accordance with the current International Council for Harmonisation (ICH) guidelines on Good Clinical Practice (GCP) and

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Good Manufacturing Practice and will include any locally required statements. If necessary, labels will be translated into the local language.

7.5 Handling and storage requirements

The investigational devices that house IMP must be securely stored at 2ºC to 8ºC (ie, in a refrigerator), that is either in a locked room or in the pharmacy. Appropriate storage conditions must be ensured by controlling refrigerator temperature by using either an automated temperature monitoring and recording system or a minimum/maximum thermometer and completing a daily temperature log in accordance with local requirements. If an out-of-range temperature is noted, the Sponsor or designee must be notified so that a determination can be made whether the product should be used or not.

The Investigator or hospital pharmacist is responsible for the appropriate storage and accountability of the investigational device at the site, as well as, for the documentation of appropriate storage and accountability. Refer to the IMP Handling Manual for additional information on handling and storage requirements.

7.6 Drug and device accountability

The Investigator will receive numbered treatments that will be assigned to eligible subjects by an IRT at Baseline. All IMP administrations will be observed by the Investigator or his/her appropriately trained designee.

Appropriate accountability forms that reflect the receipt and use of the IMP and the investigational devices will be supplied to the investigational site. Details of any loss of the self-injection investigational devices due to breakage or wastage, non-use, destruction at the study site, or return to the Sponsor or designee must also be recorded on these forms. All supplies and pharmacy documentation must be made available throughout the study for UCB (or designee) to review.

The Investigator (or designee) is responsible for retaining all used, unused, and partially used IMP and investigational devices until returned to UCB. Used or partially used devices are to be stored at room temperature in a secured area and may only be destroyed following UCB's instruction. Devices with noted deficiencies are to be returned to UCB immediately. The Investigator may assign some of the Investigator's duties for drug accountability at the study site to an appropriate pharmacist/designee.

The IMP and investigational devices intended for the study cannot be used for any other purpose than that described in this protocol.

7.7 Procedures for monitoring subject 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. Subject compliance will be reported in the PS0014 study.

7.8 Concomitant medications/treatments

Any specifications given in PS0014 regarding permitted and prohibited concomitant medications must be followed.

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7.8.1 Permitted concomitant treatments (medications and therapies)

Unless otherwise specified in PS0014, subjects are permitted to continue their prescribed medical therapy for the disease in accordance with the instructions of their treating physician. Concomitant medications and therapies, including over-the-counter products and supplements, must be recorded in the subject's notes (source documentation) and provided on the eCRF. This record should include the name of the drug, the dose, the route and date(s) of administration, and the indication for use.

7.8.2 Prohibited concomitant treatments (medications and therapies)

In addition to the prohibited treatments described in PS0014, subjects are not permitted to use topical analgesics at the injection site at Baseline or Week 8 in the DV0002 substudy.

7.9 Blinding

This is an open-label substudy.

7.10 Randomization and numbering of subjects

The same unique 5-digit identification number used in the feeder study will be used in PS0014 and in substudy DV0002. This subject number will be used to identify the subject throughout PS0014 and DV0002 and to maintain subject confidentiality. At study visits, an IRT will assign the applicable subject kits of IMP. Further instructions will be provided in the IRT manual.

The IRT will generate individual assignments for the self-injection investigational devices. Eligible subjects will be assigned to the investigational devices based on a predetermined production randomization and/or packaging schedule provided by UCB (or designee). In the 1mL device cohort, all eligible subjects will be randomly assigned to perform self-injection using either the bimekizumab-SS-1mL or the bimekizumab-AI-1mL at a 1:1 ratio. The IRT will allocate kit numbers to the subject based on the subject number during the study.

Once the 1mL device cohort has finished enrolling, the 2mL device cohort will start enrolling. Eligible subjects in the 2mL device cohort will be randomly assigned to perform self-injection using either the bimekizumab-SS-2mL or bimekizumab-AI-2mL device at a 1:1 ratio. The IRT will allocate kit numbers to the subject based on the subject number during the study.

Subject numbers and kit numbers will be tracked via the IRT.

8 STUDY PROCEDURES BY VISIT

A general overview of the study assessments for the DV0002 substudy 1mL device cohort is provided in Table 5-3. Although Table 5-3 contains assessments for both DV0002 and PS0014, it also indicates which assessments are specific to the DV0002 substudy. The lists of procedures at each study visit for the 1mL device cohort are described in Section 8.1.

For subjects in the 2mL device cohort, Baseline for DV0002 can correspond to the PS0014 Week 24, Week 28, or Week 32 visits for subjects receiving bimekizumab Q4W or to the PS0014 Week 14 or Week 32 visits for subjects receiving bimekizumab Q8W. For the 2mL device cohort, the schedule of assessments for PS0014 is presented in Table 5-4. The additional assessments to be performed for the DV0002 substudy specifically are presented in Table 5-5 and the list of procedures at each study visit is described in Section 8.2.

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Of note, DV0002 and PS0014 will share a common database/eCRF system (including common AE reporting) and a common IRT.

The following visit windows are permitted:

- As in PS0014, a 7-day visit window on either side of the scheduled dosing is permitted; however, the Investigator should try to keep the subjects on the original dosing schedule. Changes to the dosing schedule outside of the 7-day window must be discussed with the Medical Monitor.
- The SFU telephone call should occur within 7 days after the last dose in the DV0002 substudy, ±3 days.

8.1 Treatment Period for the 1mL Device Cohort

The DV0002 substudy will include all PS0014 study assessments from Baseline to Week 16 (inclusive). For subjects in the 1mL device cohort, Baseline for DV0002 corresponds to Baseline in PS0014.

8.1.1 Visit 1 (Baseline)

The following procedures/assessments will be performed:

- Obtain written informed consent (may be obtained prior to Visit 1).
- Verification of inclusion/exclusion criteria.
- Physical examination (including evaluation for signs and symptoms of tuberculosis [TB] and risk of exposure to TB).
- Body weight.
- Vital signs (sitting systolic blood pressure [BP], diastolic BP, pulse rate, and body temperature).
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry.
  - Urinalysis.
  - Urine drug screen.
  - Urine pregnancy test.
  - Bimekizumab plasma concentration.
  - Anti-bimekizumab antibodies.
- Electrocardiogram (ECG).
- TB questionnaire.
- Psoriasis Area Severity Index (PASI).
- Percentage of body surface area (BSA).

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- Investigator's Global Assessment (IGA).
- Dermatology Life Quality Index.
- Patient Health Questionnaire 9 (PHQ-9).
- Electronic Columbia Suicide Severity Rating Scale (eC-SSRS).
- Modified Nail Psoriasis Severity Index for subjects with nail involvement at Baseline in the feeder study.
- Scalp IGA for subjects with scalp involvement at Baseline in the feeder study.
- Palmoplantar Investigator's Global Assessment for subjects with palmoplantar involvement at Baseline in the feeder study.
- Euro-Quality of Life 5-Dimensions 3-level.
- Short Form 36-item Health Survey.
- Patient Global Assessment of PSO.
- Psoriatic Arthritis Screening and Evaluation.
- Patient Global Assessment of Disease Activity (only for subjects with psoriatic arthritis).
- Work Productivity and Activity Impairment Questionnaire-specific health problem v2.0.
- Concomitant medication.
- Recording of AEs.
- IRT contact.
- Random assignment to self-injection investigational device (DV0002-specific).
- Subject training for VAS and SIAQ Questionnaire (DV0002-specific).
- Complete the pre-injection SIAQ Questionnaire (version 2.0 for bimekizumab-SS-1mL and version 2.1 for bimekizumab-AI-1mL) (DV0002-specific).
- Subject training for self-injection (DV0002-specific).
- Subject self-injection of bimekizumab (DV0002-specific).
- Study personnel evaluation of self-injection (DV0002-specific).
- Study personnel evaluation of post-use device for structural/mechanical integrity (DV0002-specific).
- Complete the VAS for injection site pain (DV0002-specific).
- Complete the post-injection SIAQ Questionnaire (version 2.0 for bimekizumab-SS-1mL and version 2.1 for bimekizumab-AI-1mL) (DV0002-specific).
- Drug and device accountability (DV0002-specific).

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8.1.2 Visit 2 (Week 4)

The following procedures/assessments will be performed:

- Vital signs (sitting systolic BP, diastolic BP, pulse rate, and body temperature).
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry.
  - Urinalysis.
  - Urine pregnancy test.
  - Bimekizumab plasma concentration (for subjects with bimekizumab Q4W dosing) (DV0002-specific).
- PASI.
- Percentage of BSA.
- IGA.
- PHQ-9.
- eC-SSRS.
- Concomitant medication.
- Recording of AEs.
- IRT contact.
- Study personnel administration of bimekizumab using a 1mL PFS (for subjects with bimekizumab Q4W dosing).
- Drug and device accountability (DV0002-specific).

8.1.3 Visit 3 (Week 8)

The following procedures/assessments will be performed:

- Vital signs (sitting systolic BP, diastolic BP, pulse rate, and body temperature).
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry.
  - Urinalysis.
  - Urine pregnancy test.
  - Bimekizumab plasma concentration (DV0002-specific).
- PASI.
- Percentage of BSA.

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- IGA.
- PHQ-9.
- eC-SSRS.
- Concomitant medication.
- Recording of AEs.
- IRT contact.
- Subject self-injection of bimekizumab (DV0002-specific).
- Study personnel evaluation of self-injection (DV0002-specific).
- Study personnel evaluation of post-use device for structural/mechanical integrity (DV0002-specific).
- Complete the VAS for injection site pain (DV0002-specific).
- Complete the post-injection SIAQ Questionnaire (version 2.0 for bimekizumab-SS-1mL and version 2.1 for bimekizumab-AI-1mL) (DV0002-specific).
- Drug and device accountability (DV0002-specific).

8.1.4 Visit 3a (Week 9; safety follow-up telephone call)

Visit 3a (Week 9) will occur in the DV0002 substudy, but not in the PS0014 study. The following procedures/assessments will be performed:

- Concomitant medication (DV0002-specific).
- Recording of AEs and ADEs (DV0002-specific).

8.1.5 Visit 4 (Week 12)

The following procedures/assessments will be performed:

- Physical examination (including evaluation for signs and symptoms of TB and risk of exposure to TB).
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Urine pregnancy test.
  - Bimekizumab plasma concentration (for subjects with bimekizumab Q4W dosing) (DV0002-specific).
- TB questionnaire.
- PASI.
- Percentage of BSA.
- IGA.

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- Concomitant medication.
- Recording of AEs.
- IRT contact.
- Study personnel administration of bimekizumab using a 1mL PFS (for subjects with bimekizumab Q4W dosing).
- Drug and device accountability (DV0002-specific).

8.1.6 Visit 5 (Week 16)

The following procedures/assessments will be performed:

- Vital signs (sitting systolic BP, diastolic BP, pulse rate, and body temperature).
- Collection of blood and urine samples for the following clinical laboratory tests should be obtained prior to dosing:
  - Hematology and chemistry.
  - Urinalysis.
  - Urine pregnancy test.
  - Bimekizumab plasma concentration for subjects on bimekizumab Q8W dosing.
  - Anti-bimekizumab antibody plasma concentration for subjects on Q4W and Q8W dosing.
- PASI.
- Percentage of BSA.
- IGA.
- PHQ-9.
- eC-SSRS.
- Concomitant medication.
- Recording of AEs.
- IRT contact.
- Study personnel administration of bimekizumab using a 1mL PFS.
- Drug and device accountability (DV0002-specific).

8.2 Treatment Period for 2mL Device Cohort

For the 2mL device cohort, DV0002 Visit 1 (Baseline) will occur at PS0014 Week 24, Week 28, or Week 32 for subjects receiving bimekizumab Q4W or Week 24 or Week 32 for subjects receiving bimekizumab Q8W.

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8.2.1 Visit 1 (Baseline)

For DV0002 Visit 1 (Baseline) study assessments, refer to Table 5-4 and perform the assessments for the week that the subject starts the DV0002 substudy (PS0014 Week 24, Week 28, or Week 32 for bimekizumab Q4W or Week 24 or Week 32 for bimekizumab Q8W). In addition to the PS0014 study assessments, the following assessments will be performed at the Baseline visit of DV0002 (Table 5-5):

- Informed consent for DV0002.
- Random assignment to device (DV0002-specific).
- IRT contact.
- Blood sample for bimekizumab plasma concentrations.
- Subject training for VAS and SIAQ Questionnaire (version 2.0 for bimekizumab-SS-2mL and version 2.1 for bimekizumab-AI-2mL) (DV0002-specific).
- Complete the pre-injection SIAQ Questionnaire (DV0002-specific).
- Subject training for self-injection (DV0002-specific).
- Subject self-injection of bimekizumab using the assigned device (DV0002-specific).
- Study personnel evaluation of self-injection (DV0002-specific).
- Complete the VAS for injection site pain (DV0002-specific).
- Complete the post-injection SIAQ Questionnaire (version 2.0 for bimekizumab-SS-2mL and version 2.1 for bimekizumab-AI-2mL) (DV0002-specific).
- Study personnel evaluation of device for structural/mechanical integrity (DV0002-specific).
- Drug and device accountability (DV0002-specific).

8.2.2 Visit 2 (Baseline + 4 weeks)

For PS0014 study assessments, refer to Table 5-4. In addition, perform the following DV0002 substudy assessments:

- IRT contact
- Blood sample for bimekizumab plasma concentrations (DV0002-specific)—only done for subjects who receive bimekizumab Q4W
- Bimekizumab administration by study personnel using the PFS—only done for subjects who receive bimekizumab Q4W.
- Drug and device accountability (DV0002-specific)—only done for subjects who receive bimekizumab Q4W.

8.2.3 Visit 3 (Baseline + 8 weeks)

For PS0014 study assessments, refer to Table 5-4. In addition, perform the following DV0002 substudy assessments:

- IRT contact.

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- Blood sample for bimekizumab plasma concentrations (DV0002-specific).
- Subject self-injection of bimekizumab using the assigned device (DV0002-specific).
- Study personnel evaluation of self-injection (DV0002-specific).
- Complete the VAS for injection site pain (DV0002-specific).
- Complete the post-injection SIAQ Questionnaire (version 2.0 for bimekizumab-SS-2mL and version 2.1 for bimekizumab-AI-2mL) (DV0002-specific).
- Study personnel evaluation of device for structural/mechanical integrity (DV0002-specific).
- Drug and device accountability (DV0002-specific).

8.2.4 Visit 3a (Baseline + 9 weeks; safety follow-up telephone call)

Visit 3a (Week 9) will occur in the DV0002 substudy but not in the PS0014 study. The following procedures/assessments will be performed:

- Concomitant medications.
- Adverse events.

8.2.5 Visit 4 (Baseline + 12 weeks)

For PS0014 study assessments, refer to Table 5-4. In addition, perform the following DV0002 substudy assessments:

- IRT contact.
- Blood sample for bimekizumab plasma concentrations (DV0002-specific)—only done for subjects who receive bimekizumab Q4W.
- Bimekizumab administration by study personnel using the PFS—only done for subjects who receive bimekizumab Q4W.
- Drug and device accountability (DV0002-specific).

8.2.6 Visit 5 (Baseline + 16 weeks)

For PS0014 study assessments, refer to Table 5-4. In addition, perform the following DV0002 substudy assessments:

- IRT contact.
- Blood sample for bimekizumab plasma concentrations (DV0002-specific)—only done for subjects who receive bimekizumab Q8W.
- Bimekizumab administration by study personnel using the PFS. (If this visit coincides with Week 48 of PS0014, subjects will have the option to self-inject; refer to the PS0014 protocol.)
- Drug and device accountability (DV0002-specific).

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9 ASSESSMENT OF SELF-INJECTION

Evaluation of dose delivery and safe self-injection will be performed as described for the primary outcome variable (Section 4.1.1).

9.1 Assessment of self-injection experience by SIAQ

The SIAQ will be used to assess the subject's self-injection experience.

The SIAQ was developed by UCB to assess the perceived advantages and the potential limitations of self-injection of an sc medication (Keininger and Coteur, 2011). The pre-injection SIAQ is composed of 7 items grouped into 3 domains (feelings about injection, self-confidence, and satisfaction with the current mode of administration). The post-injection SIAQ is composed of 21 items grouped into 6 domains (feelings about injection, self-image, self-confidence, injection site reactions, ease of use, and satisfaction with self-injection). The pre-injection SIAQ will be completed at Visit 1, and the post-injection SIAQ will be completed within 30 minutes after self-injection (ie, at Visit 1 and Visit 3). For the 1mL device cohort, the SIAQ will be completed within 30 minutes of completing the second injection. For the 2mL device cohort, the SIAQ will be completed within 30 minutes of completing the single injection.

Version 2.0 and version 2.1 of the SIAQ are identical, except for Question 11. In version 2.0 of the SIAQ, Question 11 discusses the use of a plunger, while in version 2.1 of the SIAQ, Question 11 discusses depression of the device. Version 2.0 will therefore be used to assess bimekizumab-SS-1mL and bimekizumab-SS-2mL, while version 2.1 will be used to assess bimekizumab-AI-1mL and bimekizumab-AI-2mL.

9.2 Assessment of injection site pain

A VAS will be used to assess overall injection pain due to self-injection at DV0002 Baseline and at 8 weeks after training. Subjects will be required to indicate their injection pain by placing a mark on a 100mm line from 0 (no pain) to 100 (worst possible pain).

1mL Device Cohort

In the 1mL device cohort of the DV0002 substudy, the 320mg bimekizumab dose will be administered as two 160mg sc injections with either 2 bimekizumab-SS-1mL or 2 bimekizumab-AI-1mL devices. To evaluate injection pain for both self-injections, the VAS will be assessed immediately (within 15 minutes) after completion of the second self-injection. The subject will complete the VAS prior to completion of the post-injection SIAQ (refer to Section 9.1 for details).

2mL Device Cohort

In the 2mL device cohort, the 320mg bimekizumab dose will be administered as 1 sc injection with either the bimekizumab-SS-2mL or bimekizumab-AI-2mL device. To evaluate injection pain for the self-injection, the VAS will be assessed immediately (within 15 minutes) after completion of the self-injection. The subject will complete the VAS prior to completion of the post-injection SIAQ (refer to Section 9.1 for details).

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9.3 Evaluation of post-use structural and mechanical integrity of self-injection investigational devices

The visual inspection of the used devices will check for structural/mechanical integrity and damage (ie, clear evidence of damage/compromised structural integrity and not any superficial, cosmetic imperfections). All evaluations will be performed by appropriately trained site staff. Any device with structural/mechanical integrity issues will be returned to UCB for further evaluation. Superficial, cosmetic imperfections which have no impact on structural or mechanical integrity are to be ignored.

Used devices that functioned as intended and which had no post-use structural or mechanical integrity issues (as determined by the post-use site evaluation) will also be returned to UCB for further evaluation.

10 ASSESSMENT OF PHARMACOKINETIC VARIABLES

1mL Device Cohort

Blood samples for measurement of trough bimekizumab PK (Section 4.1.3.2) will be collected at the time points specified in the schedule of study assessments (Table 5-3).

At dosing visits, blood samples will be drawn prior to dosing (at the same time of the sampling for clinical laboratory tests). The time and date of collection will be recorded in the eCRF.

Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the laboratory manual for this study. Detailed information on sample analysis will be provided in a bioanalytical report.

2mL Device Cohort

For subjects who participate in the 2mL device cohort, blood samples for measurement of trough bimekizumab PK levels (Section 4.1.3.2) will be collected at the timepoints specified in Table 10-1.

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Table 10-1: DV0002 substudy 2mL device cohort PK sample collection time points

Dose Regimen	PS0014 Week that subject starts DV0002	DV0002 Visits				
		Visit 1 (Baseline)/ Week 0	Visit 2/ Week 4	Visit 3/ Week 8	Visit 4/ Week 12	Visit 5/ Week 16
320mg Q4W	Week 24	X[a]	X	X	X	X[a]
	Week 28	X	X	X	X[a]	NA
	Week 32	X	X	X[a]	X	X[a]
320mg Q8W	Week 24	X[a]	NA	X	NA	X[a]
	Week 32	X	NA	X[a]	NA	X[a]

NA=not applicable; PK=pharmacokinetics; Q4W=every 4 weeks; Q8W=every 8 weeks
Note: For the 2mL device cohort, the DV0002 Baseline visit will be PS0014 Week 24, Week 28, or Week 32 for subjects receiving bimekizumab 320mg Q4W or PS0014 Week 24 or Week 32 for subjects receiving bimekizumab 320mg Q8W.
[a] PK sample taken per the PS0014 schedule.

At dosing visits, blood samples will be drawn prior to dosing (at the same time of the sampling for clinical laboratory tests). The time and date of collection will be recorded in the eCRF.

Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the laboratory manual for this study. Detailed information on sample analysis will be provided in a bioanalytical report.

11 ASSESSMENT OF SAFETY

11.1 Adverse events (investigational device)

All AEs (including serious adverse events [SAEs]) will be reported in a common database for PS0014 and DV0002, but only ADEs, SADEs, and device deficiencies will be summarized in the DV0002 substudy. Specifically, only those AEs related to the use of the investigational medical devices (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; please refer to the PS0014 protocol for information on reporting and recording AEs (including SAEs).

11.1.1 Definitions (investigational device)

11.1.1.1 Adverse device effect (investigational device)

An ADE is an 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 IFU, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device.

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- Adverse event that is a result of a use error or intentional misuse of the investigational device.

11.1.1.1.1 Unanticipated adverse device effect

An unanticipated ADE is an ADE which by its nature, incidence, severity, or outcome has not been previously identified.

11.1.1.2 Serious adverse device effects

A SADE is an ADE that has resulted in any of the consequences characteristic of an SAE.

An SAE (and therefore a SADE) must meet 1 or more of the following criteria:

- Death
- Life-threatening

  (Life-threatening does not include a reaction that might have caused death had it occurred in a more severe form.)
- Significant or persistent disability/incapacity
- Congenital anomaly/birth defect (including that occurring in a fetus)
- Important medical event that, based upon appropriate medical judgment, may jeopardize the patient or subject and may require medical or surgical intervention to prevent 1 of the other outcomes listed in the definition of serious

  (Important medical events may include, but are not limited to, potential Hy's Law, allergic bronchospasm requiring intensive treatment in an emergency room or at home, blood dyscrasias that do not result in inpatient hospitalization, or the development of drug dependency or drug abuse.)
- Initial inpatient hospitalization or prolongation of hospitalization

  (A patient admitted to a hospital even if he/she is released on the same day, meets the criteria for the initial inpatient hospitalization. An emergency room visit that results in admission to the hospital would also qualify for the initial inpatient hospitalization criteria. However, emergency room visits that do not result in admission to the hospital would not qualify for these criteria and, instead, should be evaluated for 1 of the other criteria in the definition of serious [eg, life-threatening adverse experience, important medical event].

  Hospitalizations for reasons not associated with the occurrence of an AE [eg, preplanned surgery or elective surgery for a pre-existing condition that has not worsened or manifested in an unusual or uncharacteristic manner] do not qualify for reporting. For example, if a subject has a condition recorded on his/her medical history and later has a preplanned surgery for this condition, it is not appropriate to record the surgery or hospitalization as an SAE, since there is no AE upon which to assess the serious criteria. Please note that, if the pre-existing condition has worsened or manifested in an unusual or uncharacteristic manner, this would then qualify as an AE and, if necessary, the seriousness of the event would need to be determined.)

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11.1.1.2.1 Anticipated and unanticipated serious adverse device effects

An anticipated SADE is a SADE which by its nature, incidence, severity, or outcome has been identified in the risk analysis report (ISO 14155).

An unanticipated serious adverse device effect (USADE) is a SADE which by its nature, incidence, severity, or outcome has not been identified in the current version of the risk analysis report.

The Sponsor will determine if a SADE qualifies as an USADE. The Sponsor will also evaluate all SADEs to ensure that expedited reporting requirements are met according to UCB Standard Operating Procedures (SOPs) and applicable country-specific regulatory requirements for the investigational device.

11.1.1.3 Device deficiency (investigational device)

A device deficiency is an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety, or performance. Device deficiencies include malfunctions, use errors, and inadequate labeling.

11.1.2 Procedures for reporting and recording adverse device effects and device deficiencies

The subject will be given the opportunity to report ADEs, SADEs and device deficiencies spontaneously. A general prompt will also be given at each study visit to detect AEs that qualify as ADEs, SADEs, and device deficiencies. Below is an example prompt:

"Did you notice anything unusual about the injection?"

11.1.2.1 Reporting of adverse device effects

All ADEs and SADEs will be captured on the eCRF. The eCRF will allow Investigators to specify whether an AE or SAE is device-related and will clarify which investigational device is associated with the ADE or SADE.

An Investigator Adverse Device Effect and Device Deficiency form will be provided to the Investigator. The Investigator Adverse Device Effect and Device Deficiency form must be completed in English.

The Investigator (or designee) shall report all SADEs and device deficiencies that might have led to an SAE (if suitable action had not been taken, if intervention had not been made, or if circumstances had been less fortunate) to UCB within 24 hours after knowledge of the event using the appropriate forms in the electronic data capture system. When required by national or local regulations, the Investigator shall also notify the IRB and regulatory agencies of all reportable events according to national regulations in acceptable timely conditions and may also be requested by the IRBs to provide annual reports.

11.1.2.2 Reporting of device deficiencies

If a device deficiency related to the identity, quality, durability, reliability, safety, or performance of the investigational device is reported (even if the investigational device was not used), UCB must be informed within 1 business day (within 24 hours, as a rule) of receipt of this information by the site. The Investigator must forward to UCB (or designee) a duly completed Investigator

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Adverse Device Effect and Device Deficiency form provided by UCB, even if the data are incomplete or if it is obvious that more data will be needed to draw any conclusions.

An Investigator Adverse Device Effect and Device Deficiency form will be provided to the Investigator. The Investigator Adverse Device Effect and Device Deficiency form must be completed in English.

It is important for the Investigator, when completing the Investigator Adverse Device Effect and Device Deficiency form, to include an assessment and documentation of whether the device deficiency could have led to an SAE if any of the following occurred:

- Suitable action had not been taken, or
- Intervention had not been made, or
- Circumstances had been less fortunate.

All defective devices must be returned to UCB according to standard procedures.

11.1.2.3 Reporting of serious adverse device effects including device deficiencies with risk of serious adverse event

If a device deficiency that could have led to an SAE (if suitable action had not been taken, or intervention had not been made, or circumstances had been less fortunate) is reported, UCB must be informed within 24 hours of receipt of this information by the site (see contact information for SAE reporting listed in the Serious Adverse Event Reporting section at the front of the protocol). The Investigator must forward to UCB (or designee) a duly completed "Investigator SAE Report Form for Investigational Medical Devices" provided by UCB, even if the data are incomplete, or if it is obvious that more data will be needed to draw any conclusions. Information recorded on this form will be entered into the global safety database.

An Investigator SAE Report Form for Investigational Medical Devices will be provided to the Investigator. The Investigator SAE Report Form for Investigational Medical Devices must be completed in English.

Additional information (eg, autopsy or laboratory reports) received by the Investigator must be provided within 24 hours. All documents in the local language must be accompanied by a translation in English, or the relevant information included in the same document must be summarized in the Investigator SAE Report Form for Investigational Medical Devices.

The Investigator is specifically requested to collect and report to UCB (or designee) any ADEs or SADEs up to completion of the follow-up visit/telephone call for each subject, and to also inform participating subjects of the need to inform the Investigator of any ADEs or SADEs within this period. Serious AEs that the Investigator thinks may be associated with the device must be reported to UCB regardless of the time between the event and the end of the study.

Upon receipt of the Investigator SAE Report Form for Investigational Medical Devices, UCB will perform an assessment of whether the SADE is anticipated based on the current version of the risk analysis report.

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11.1.2.4 Rule for repetition of an adverse device effect, serious adverse device effect, and/or device deficiency

An increase in the intensity of an ADE or SADE should lead to the repetition of the ADE or SADE being reported with:

- The outcome date of the first ADE or SADE that is not related to the natural course of the disease being the same as the start date of the repeated ADE or SADE, and the outcome of "worsening."
- The ADE or SADE verbatim term being the same for the first and repeated ADE or SADE, so that the repeated ADE or SADE can be easily identified as the worsening of the first one.

11.1.3 Follow up of adverse device effects and serious adverse device effects

All ADEs and SADEs should be followed until they have resolved, have stable sequelae, the Investigator determines that they are no longer clinically significant, or the subject is lost to follow up.

If an ADE or SADE is ongoing at the end of the study for a subject, follow up should be provided until resolution/stable level of sequelae is achieved, or until the Investigator no longer deems that it is clinically significant, or until the subject is lost to follow up. If no follow up is provided, the Investigator must provide a justification.

Information on SADEs obtained after clinical database lock will be captured through the Patient Safety (PS) database without limitation of time.

11.2 Pregnancy

All events of pregnancy or partner pregnancy will be followed and documented as described in the PS0014 protocol.

11.3 Suspected transmission of an infectious agent

For the purposes of reporting, any suspected transmission of an infectious agent via medicinal products (device or IMP) should be considered as an SAE or SADE; such cases must be reported immediately, recorded in the Adverse Event module of the eCRF, and followed as any other SAE or SADE. Any organism, virus, or infectious particle (eg, prion protein transmitting transmissible spongiform encephalopathy), pathogenic or nonpathogenic, is considered an infectious agent.

There is no evidence that there is a risk of transmission of an infectious agent with the investigational device.

11.4 Overdose of investigational medicinal product

Excessive dosing (beyond that prescribed in the protocol and including overdose) should be recorded in the eCRF. Any SADE or nonserious ADE associated with excessive dosing must be followed as any other SADE or nonserious ADE. These events are only considered ADEs or SADEs if there are associated clinical signs and symptoms or if the act of taking the excess medicine itself is an ADE or SADE (eg, suicide attempt).

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There is no evidence that there is a risk of overdose with the IMP when used with the investigational device.

11.5 Safety signal detection

Selected data from this study will be reviewed periodically to detect, as early as possible, any safety concern(s) related to the IMP or the investigational device so that Investigators, clinical study subjects, regulatory authorities, and IRBs will be informed appropriately and as early as possible.

The Study Physician (or medically qualified designee/equivalent) will conduct an ongoing review of SADEs and will perform ongoing SADE reconciliations in collaboration with the PS representative. Serious AEs not related to a device will be reported in PS0014.

As appropriate for the stage of development and accumulated experience with the IMP and the investigational device, medically qualified personnel at UCB may identify additional safety measures (ie, vital signs) for which data will be periodically reviewed during the study.

11.6 Other safety measurements

11.6.1 Vital signs measurement

No vital sign assessments will be performed for the DV0002 substudy. The vital sign assessments presented in Table 5-3, Table 5-4, and Section 8 will be captured as part of the PS0014 study and are described in the PS0014 protocol.

12 EFFICACY ASSESSMENTS FOR PS0014

No efficacy assessments will be performed for the DV0002 substudy. The efficacy assessments presented in Table 5-3, Table 5-4, and Section 8 will be captured as part of the PS0014 study and are described in the PS0014 protocol.

13 STUDY MANAGEMENT AND ADMINISTRATION

13.1 Adherence to protocol

The Investigator should not deviate from the DV0002 protocol or the PS0014 protocol. However, the Investigator should take any measure necessary, in deviation from or not defined by the protocol, in order to protect clinical study subjects from any immediate hazard to their health and safety. In this case, this action should be taken immediately, without prior notification of the regulatory authority, IRB, or Sponsor.

After implementation of such measure, the Investigator must notify the Clinical Project Manager of the Sponsor within 24 hours and follow any local regulatory requirements.

13.2 Monitoring

UCB (or designee) will monitor the study to meet the Sponsor's monitoring SOPs, ICH-GCP guidelines, and applicable regulatory requirements, and to ensure that study initiation, conduct, and closure are adequate. Monitoring of the study may be delegated by UCB to a contract research organization (CRO) or a contract monitor.

The Investigator and his/her staff are expected to cooperate with UCB (or designee) and to be available during the monitoring visits to answer questions sufficiently and to provide any

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missing information. The Investigator(s)/institution(s) will permit direct access to source data/documents for study-related monitoring, audits, IRB review, and regulatory inspection(s).

The Investigator will allow UCB (or designee) to periodically review all eCRFs and corresponding source documents (eg, hospital and laboratory records for each study participant). Monitoring visits will provide UCB (or designee) with the opportunity to evaluate the progress of the study, verify the accuracy and completeness of eCRFs, ensure that all protocol requirements, applicable authorities' regulations, and Investigator's obligations are being fulfilled, and resolve any inconsistencies in the study records.

13.2.1 Definition of source data

All source documents must be accurate, clear, unambiguous, permanent, and capable of being audited. They should be made using some permanent form of recording (ink, typing, printing, optical disc). They should not be obscured by correction fluid or have temporary attachments (such as removable self-stick notes).

Source documents are original records in which raw data are first recorded. These may include hospital/clinic/general practitioner records, charts, diaries, x-rays, laboratory results, printouts, pharmacy records, care records, ECG or other printouts, completed scales, or quality of life questionnaires, for example. Source documents should be kept in a secure, limited access area.

Source documents that are computer generated and stored electronically must be printed for review by the monitor (eg, ECG reports). Once printed, these copies should be signed and dated by the Investigator and become a permanent part of the subject's source documents. The Investigator will facilitate the process for enabling the monitor to compare the content of the printout and the data stored in the computer to ensure all data are consistent.

Electronic data records, such as Holter monitor records or electroencephalogram records, must be saved and stored as instructed by UCB (or designee).

13.2.2 Source data verification

Source data verification ensures accuracy and credibility of the data obtained. During monitoring visits, reported data are reviewed with regard to being accurate, complete, and verifiable from source documents (eg, subject files, recordings from automated instruments, tracings [ECG], x-ray films, laboratory notes). All data reported on the eCRF should be supported by source documents, unless otherwise specified in Section 13.2.1.

13.3 Data handling

13.3.1 Case Report form completion

This study is performed using remote data capture; the same data capture is used for PS0014 and DV0002. The Investigator is responsible for prompt reporting of accurate, complete, and legible data in the eCRFs and in all required reports.

Any change or correction to the eCRF after saving must be accompanied by a reason for the change.

Corrections made after the Investigator's review and approval (by means of a password/electronic signature) will be reapproved by the Investigator.

The Investigator should maintain a list of personnel authorized to enter data into the eCRF.

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Detailed instructions will be provided in the eCRF Completion Guidelines.

13.3.2 Database entry and reconciliation

Case Report forms/external electronic data will be entered/loaded into a validated electronic database using a clinical data management system (CDMS). Computerized data cleaning checks will be used, in addition to manual review, to check for discrepancies and to ensure consistency of the data. The data are entered into the eCRFs once and are subsequently verified.

An electronic audit trail system will be maintained within the CDMS to track all data changes in the database once the data have been saved initially into the system or electronically loaded. Regular backups of the electronic data will be performed.

13.3.3 Subject Screening and Enrollment log/Subject Identification Code list

The subject's screening and enrollment will be recorded in the Subject Screening and Enrollment log.

The Investigator will keep a Subject Identification Code list. This list will remain with the Investigator and be used for unambiguous identification of each subject.

The subject's consent and enrollment in the study must be recorded in the subject's medical record. These data should identify the study and document the dates of the subject's participation.

13.4 Termination of the study

UCB reserves the right to temporarily suspend or prematurely discontinue this study either at a single site, multiple sites, or at all sites at any time for reasons including, but not limited to, safety or ethical issues, inaccurate or incomplete data recording, noncompliance, or unsatisfactory enrollment with respect to quality or quantity.

The study may also be temporarily suspended or prematurely terminated in either of the following situations:

- Severe or serious injection site reaction (eg, bleeding, bruising, pain) that, in the opinion of the Investigator, the overseeing IRB, or the Sponsor, is likely to be seen in other enrolled subjects who have not yet been injected with bimekizumab.
- Unexpected device malfunction leading to a failed or incomplete injection, or resulting in an SAE that, in the opinion of the Investigator, the overseeing IRB, or the Sponsor, is likely to be seen in other enrolled subjects who have not yet been injected with bimekizumab.

If the study is prematurely terminated or suspended, UCB (or designee) will inform the Investigators/institutions and the regulatory authority(ies) of the termination or suspension and the reason(s) for the termination or suspension, in accordance with applicable regulatory requirement(s). The IRB should also be informed and provided with reason(s) for the termination or suspension by the Sponsor or by the Investigator/institution, as specified by the applicable regulatory requirement(s). In addition, arrangements will be made for the return of all unused IMP and other material in accordance with UCB procedures for the study.

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13.5 Archiving and data retention

The Investigator will maintain adequate records for the study, including eCRFs, medical records, laboratory results, informed consent documents, drug dispensing and disposition records, safety reports, information regarding participants who discontinued, and other pertinent data.

All essential documents are to be retained by the Investigator until at least 2 years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region, or at least 2 years have elapsed since the formal discontinuation of clinical development of the IMP or investigational device. These documents should be retained for a longer period; however, if required by the applicable regulatory requirement(s) or by an agreement with UCB (CPMP/ICH/135/95, 2002 [Section 4.9.5]). The Investigator will contact UCB for authorization prior to the destruction of any study records or in the event of accidental loss or destruction of any study records. The Investigator will also notify UCB should he/she relocate or move the study-related files to a location other than that specified in the Sponsor's trial master file.

13.6 Audit and inspection

The Investigator will permit study-related audits mandated by UCB, after reasonable notice, and inspections by domestic or foreign regulatory authorities.

The main purposes of an audit or inspection are to confirm that the rights and well-being of the subjects enrolled have been protected, that enrolled subjects (ie, signing consent and undergoing study procedures) are appropriate for the study, and that all data relevant for the evaluation of the IMP and the investigational device have been processed and reported in compliance with the planned arrangements, the protocol, investigational site, and IRB SOPs, ICH GCP, and applicable regulatory requirements.

The Investigator will provide direct access to all study documents, source records, and source data. If an inspection by a regulatory authority is announced, the Investigator will immediately inform UCB (or designee).

13.7 Good Clinical Practice

Noncompliance with the protocol, ICH-GCP, or local regulatory requirements by the Investigator, institution, institution staff, or designees of the Sponsor will lead to prompt action by UCB to secure compliance. Continued noncompliance may result in the termination of the site's involvement in the study.

14 STATISTICS

A description of statistical methods follows and will be described in more detail in the Statistical Analysis Plan (SAP).

Once subjects in the 1mL device cohort complete DV0002, a final analysis for that cohort will be performed, and a clinical study report will be prepared. A separate final analysis will be performed for the 2mL device cohort.

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14.1 Definition of analysis sets

1mL Device Cohort

For the 1mL device cohort, 2 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.

Two different Full Analysis Sets (FASs) will be generated (1 for each device type): the bimekizumab-SS-1mL Full Analysis Set (FAS-s) and the bimekizumab-AI-1mL Full Analysis Set (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.

For the PK analyses, 2 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 1 evaluable PK assessment.

2mL Device Cohort

For the 2mL device cohort, the same analysis sets will be generated.

14.2 General statistical considerations

This is an estimation study design with no formal statistical hypothesis testing. The study will estimate the true population proportion and/or mean of self-injection related endpoints for each device separately. Summary statistics for continuous variables will include: number of available observations, mean, standard deviation, minimum, median, and maximum. For categorical variables, the number and proportion of subjects, along with the 90% confidence interval (CI) based on the Exact Binomial method, will be presented.

The Baseline value is defined as the last nonmissing measurement prior to the first self-injection at DV0002 Visit 1 (Baseline). No imputation of missing data will be performed. All data recorded in the eCRF and questionnaires will be listed.

14.3 Planned analyses of outcome variables

All statistical analyses will be descriptive in nature. No inferential statistical analyses are planned.

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

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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.

14.3.1 Analysis of the primary outcome variable

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 (8 weeks after training). Safe and effective self-injection will be evaluated by the study personnel as defined in in Section 4.1.1.

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 using the relevant FAS population (FAS-s or FAS-a). The 90% CIs based on the Exact Binomial method will be reported as well.

14.3.2 Analysis of the secondary outcome variable

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 as defined in Section 4.1.1.

The secondary outcome variables will be analyzed in the same manner as the primary outcome variable (see Section 14.3.1).

14.3.3 Analysis of other outcome variables

The other outcome variables are defined in Section 4.1.3. These variables will be summarized using descriptive statistics and they will be tabulated separately for each device overall and within each device by dosing regimen using the relevant FAS population (FAS-s or FAS-a).

14.4 Planned pharmacokinetic analyses

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. Three BMI categories will be defined based on tertiles derived from subjects' Baseline BMI values within the device-specific population (PK-PPS-s or PK-PPS-a).

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 Week 8 for the study personnel administration and at DV0002 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 DV0002 Baseline for the study personnel administration and at 8 weeks after training (DV0002 Week 8) and DV0002 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.

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14.5 Planned safety analyses

The safety variable is the occurrence of ADEs; additional safety and tolerability variables will be collected in PS0014 (see Section 4.1.3.3). Analyses of safety data will be done separately for each device overall and within each device by dosing regimen using the relevant SS population (SS-s or SS-a).

All ADE data will be listed and no statistical testing will be performed. Only treatment-emergent ADEs will be included in the summary tables. All ADEs will be coded and classified by system organ class, high level term, and preferred term according to the latest version of the Medical Dictionary for Regulatory Activities. 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.

14.6 Planned efficacy analyses

No efficacy analyses are planned for the DV0002 substudy.

14.7 Handling of protocol deviations

Only subjects who had no important protocol deviations affecting the primary outcome variable, as confirmed during ongoing data cleaning meetings prior to database lock, will be included in the FAS-s or FAS-a. 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. To the extent feasible, the rules for identifying protocol deviations will be defined without review of the data and without consideration of the frequency of occurrence of such deviations. Whenever possible, criteria for identifying important protocol deviations will be implemented algorithmically to ensure consistency in the classification of important protocol deviations across all subjects.

14.8 Handling of dropouts or missing data

There will be no special procedures for handling missing data. All imputation of missing or partial dates for safety assessments will be detailed in the SAP.

14.9 Planned interim analysis and data monitoring

No interim analysis is planned for the DV0002 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 ADEs and ongoing concomitant medication.

14.10 Determination of sample size

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

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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 in 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.

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. 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.

15 ETHICS AND REGULATORY REQUIREMENTS

15.1 Informed consent

Subject's informed consent must be obtained and documented in accordance with local regulations, ICH-GCP requirements, and the ethical principles that have their origin in the principles of the Declaration of Helsinki.

Prior to obtaining informed consent, information should be given in a language and at a level of complexity understandable to the subject in both oral and written form by the Investigator (or designee). Each subject will have the opportunity to discuss the study and its alternatives with the Investigator.

Prior to participation in the study, the ICF should be signed and personally dated by the subject, or his/her legal representative, and by the person who conducted the informed consent discussion (Investigator or designee). The subject or his/her legal representative must receive a copy of the signed and dated ICF. As part of the consent process, each subject must consent to direct access

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to his/her medical records for study-related monitoring, auditing, IRB review, and regulatory inspection.

If the ICF is amended during the study, the Investigator (or the Sponsor, if applicable) must follow all applicable regulatory requirements pertaining to the approval of the amended ICF by the IRB and use of the amended form.

All studies conducted at centers in the US must include the use of a Health Insurance Portability and Accountability Act Authorization form.

The subject may withdraw his/her consent to participate in the study at any time. A subject is considered as enrolled in the study when he/she has signed the ICF. An eCRF must not be started, nor may any study-specific procedure be performed for a given subject, without having obtained his/her written consent to participate in the study.

15.2 Subject identification cards

Upon signing the ICF, the subject or legal representative will be provided with a subject identification card in the language of the subject. The Investigator will fill in the subject identifying information and medical emergency contact information. The Investigator will instruct the subject to keep the card with him/her at all times.

15.3 Institutional Review Boards

The study will be conducted under the auspices of an IRB, as defined in local regulations, ICH-GCP, and in accordance with the ethical principles that have their origin in the Declaration of Helsinki.

The Investigator/UCB will ensure that an appropriately constituted IRB, that complies with the requirements of the current ICH-GCP version or applicable country-specific regulations, will be responsible for the initial and continuing review and approval of the clinical study. Prior to initiation of the study, the Investigator/UCB will forward copies of the protocol, ICF, Investigator's Brochure, Investigator's curriculum vitae (if applicable), advertisement (if applicable), and all other subject-related documents to be used for the study to the IRB for its review and approval.

Before initiating a study, the Investigator will have written and dated full approval from the responsible IRB for the protocol.

The Investigator will also promptly report to the IRB all changes in the study, all unanticipated problems involving risks to human subjects or others, and any protocol deviations, to eliminate immediate hazards to subjects.

The Investigator will not make any changes in the study or study conduct without IRB approval, except where necessary to eliminate apparent immediate hazards to the subjects. For minor changes to a previously approved protocol during the period covered by the original approval, it may be possible for the Investigator to obtain an expedited review by the IRB as allowed.

As part of the IRB requirements for continuing review of approved studies, the Investigator will be responsible for submitting periodic progress reports to the IRB (based on IRB requirements), at intervals appropriate to the degree of subject risk involved, but no less than once per year. The Investigator should provide a final report to the IRB following study completion.

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UCB (or designee) will communicate safety information to the appropriate regulatory authorities and all active Investigators in accordance with applicable regulatory requirements. The appropriate IRB will also be informed by the Investigator or the Sponsor, as specified by the applicable regulatory requirements in each concerned country. Where applicable, Investigators are to provide the Sponsor (or designee) with evidence of such IRB notification.

15.4 Subject privacy

UCB staff (or designee) will affirm and uphold the subject's confidentiality. Throughout this study, all data forwarded to UCB (or designee) will be identified only by the subject number assigned at Visit 1.

The Investigator agrees that representatives of UCB, its designee, representatives of the relevant IRB, or representatives of regulatory authorities will be allowed to review that portion of the subject's primary medical records that directly concerns this study (including, but not limited to, laboratory test result reports, ECG reports, admission/discharge summaries for hospital admissions occurring during a subject's study participation, and autopsy reports for deaths occurring during the study).

15.5 Protocol amendments

Protocol changes may affect the legal and ethical status of the study and may also affect the statistical evaluations of sample size and the likelihood of the study fulfilling its primary objective.

Significant changes to the protocol will only be made as an amendment to the protocol and must be approved by UCB, the IRB, and the regulatory authorities (if required), prior to being implemented.

16 FINANCE, INSURANCE, AND PUBLICATION

Insurance coverage will be handled according to local requirements.

Finance, insurance, and publication rights are addressed in the Investigator and/or CRO agreements, as applicable.

17 REFERENCES

CPMP/ICH/135/95 Note for guidance on Good Clinical Practice (EMEA) Jul 2002.

Keininger D, Coteur C. Assessment of self-injection experience in patients with rheumatoid arthritis: psychometric validation of the Self-Injection Assessment Questionnaire (SIAQ). Health and Quality of Life Outcomes. 2011;9:2.

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18 APPENDICES

18.1 Protocol 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 protocol:

- 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:

Change #1

Section 1 Summary

DV0002 is a multicenter, open-label, randomized substudy in adult subjects with moderate to severe chronic plaque psoriasis (PSO) to evaluate the safe and effective use of 2 single-use disposable self-injecting investigational devices for the subcutaneous (sc) administration of bimekizumab solution (the investigational medicinal product [IMP]). It is expected that individuals with PSO will prefer to have options for the self-administration of bimekizumab. DV0002 will therefore evaluate 2 different self-injection investigational devices: the 1mL bimekizumab safety syringe (bimekizumab-SS-1mL) and the 1mL bimekizumab auto-injector (bimekizumab-AI-1mL).

DV0002 is a substudy of PS0014, which is a multicenter, open-label, long-term safety study for subjects with moderate to severe chronic plaque PSO who complete 1 of the Phase 3 feeder studies (PS0008, PS0009 or PS0013). The PS0014 study will evaluate the long-term safety, tolerability, and efficacy of bimekizumab in subjects with PSO, and study personnel qualified in sc injection technique will administer bimekizumab to subjects in a 1mL True North prefilled syringe (referred to throughout this protocol as the 1mL PFS). Subjects will begin the DV0002 substudy and the PS0014 study at the same time. The DV0002 substudy will include all PS0014 study assessments from Baseline to Week 16 (inclusive). However, subjects in the DV0002 substudy will self-administer bimekizumab at Baseline and at Week 8. Subjects will be randomly assigned to either the bimekizumab-SS-1mL or the bimekizumab-AI-1mL device arm.

During the 16-week Treatment Period of DV0002, subjects will receive either bimekizumab 320mg every 8 weeks (Q8W) or bimekizumab 320mg every 4 weeks (Q4W), based on their assigned dosing at Baseline. This dose regimen will remain stable for the entire 16-week Treatment Period of DV0002. In the DV0002 substudy, subjects will be assigned to 1 of the 2 self-injection investigational devices and will self-administer bimekizumab only at Baseline

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and at Week 8, regardless of their assigned dosing regimen. For subjects in the bimekizumab Q4W dosing arm, bimekizumab will be administered by study personnel at Week 4 and Week 12; for all subjects, bimekizumab will be administered by study personnel at Week 16. A safety follow-up (SFU) telephone call will occur 1 week after the last self-administration (at Week 9). 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).

To compensate for subjects who have different study treatments between the feeder studies and DV0002, DV0002 is planned to enroll approximately 200 subjects (100 subjects per device arm) to ensure that approximately 50 subjects per device arm are evaluable for steady state trough pharmacokinetic (PK) level analyses. Within each device arm, subjects will be divided into tertiles by body mass index (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.

The primary objective of the DV0002 substudy 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. 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 adverse device effects (ADEs) that would preclude continued use of the device for self-injection (ie, no serious ADEs [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 by study personnel for safety and effectiveness 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.

The secondary study objectives and other study objectives are provided in Section 3.2 and Section 3.3, respectively. Of note, one of the other study objectives is to assess trough PK 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 secondary outcome variable, other outcome variables, and the other safety variable are listed in Section 4.1.2, Section 4.1.3, and Section 4.1.3.3, respectively.

Has been changed to:

DV0002 is a multicenter, open-label, randomized substudy in adult subjects with moderate to severe chronic plaque psoriasis (PSO) to evaluate the safe and effective use of ~~24~~ **4** single-use disposable self-injection investigational devices for the subcutaneous (sc) administration of

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bimekizumab solution (the investigational medicinal product [IMP]). ~~It is expected that individuals with PSO will prefer to have options for the self-administration of bimekizumab. DV0002 will therefore evaluate 2 different self-injection investigational devices: the 1mL bimekizumab safety syringe (bimekizumab-SS-1mL) and the 1mL bimekizumab auto-injector (bimekizumab-AI-1mL).~~ **The 4 self-injection devices to be tested are the 1mL bimekizumab safety syringe (bimekizumab-SS-1mL), the 1mL bimekizumab auto injector (bimekizumab-AI-1mL), the 2mL bimekizumab safety syringe (bimekizumab-SS-2mL), and the 2mL bimekizumab auto injector (bimekizumab-AI-2ml).**

DV0002 is a substudy of PS0014, which is a multicenter, open-label, long-term safety study for subjects with moderate to severe chronic plaque PSO who complete 1 of the Phase 3 feeder studies (PS0008, PS0009, or PS0013). The PS0014 study will evaluate the long-term safety, tolerability, and efficacy of bimekizumab in subjects with PSO, and study personnel qualified in sc injection technique will administer bimekizumab to subjects in a 1mL True North prefilled syringe (referred to throughout this protocol as the 1mL PFS). ~~Subjects will begin the DV0002 substudy and the PS0014 study at the same time. The DV0002 substudy will include all PS0014 study assessments from Baseline to Week 16 (inclusive). However, subjects~~ In the DV0002 substudy, subjects will self-administer bimekizumab at **DV0002 Baseline and at DV0002** Week 8. ~~Subjects will be randomly assigned to either the bimekizumab-SS-1mL or the bimekizumab-AI-1mL device arm.~~

During the ~~16-week~~ Treatment Period of DV0002, subjects will receive either bimekizumab 320mg every 8 weeks (Q8W) or bimekizumab 320mg every 4 weeks (Q4W), based on their assigned dosing at Baseline **of PS0014. The same interactive response technology (IRT) will be used for both studies (DV0002 and PS0014).** The dose regimen will remain stable for the entire Treatment Period of DV0002.

In the DV0002 substudy, subjects will be assigned to 1 of the ~~2~~**4** self-injection ~~investigational~~ devices and will self-administer bimekizumab only at **DV0002** Baseline and at **DV0002** Week 8 **after training**, regardless of their assigned dosing regimen. ~~For subjects in the bimekizumab Q4W dosing arm, bimekizumab will be administered by study personnel at Week 4 and Week 12; for all subjects, bimekizumab will be administered by study personnel at Week 16.~~ **Bimekizumab will be administered by study personnel at DV0002 Week 4 and DV0002 Week 12 for subjects in the Q4W dosing arm and at DV0002 Week 16 for both dosing arms.** A safety follow-up (SFU) telephone call will occur 1 week after the last self-administration (at **DV0002** Week 9). 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~~).

~~To compensate for subjects who have different study treatments between the feeder studies and DV0002, DV0002 is planned to enroll approximately 200 subjects (100 subjects per device arm) to ensure that approximately 50 subjects per device arm are evaluable for steady state trough pharmacokinetic (PK) level analyses. Within each device arm, subjects will be divided into tertiles by body mass index (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.~~

The primary objective of the DV0002 substudy is to evaluate, for each device, the ability of subjects with moderate to severe chronic plaque PSO to safely and effectively self-inject

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bimekizumab 8 weeks after training in the self-injection technique. The primary 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 bimekizumab-AI-2mL device 8 weeks after training in self-injection technique (DV0002** ~~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~~ **device**, which shows that the 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 ADEs [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 by study personnel for safety and effectiveness 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.~~

The secondary study objectives and other study objectives are provided in Section 3.2 and Section 3.3, respectively. Of note, one of the other study objectives is to assess trough **pharmacokinetic (PK)** levels associated with self-injection using the ~~test~~ **investigational** device, injection by study personnel, injection site (abdomen or thigh), **and body mass index (BMI)** category (by tertile). The secondary outcome variable, other outcome variables, and the other safety variable are listed in Section 4.1.2, Section ~~4.1.3~~**4.1.3.1**, and Section 4.1.3.3, respectively.

The DV0002 substudy consists of 2 cohorts. The 1mL device cohort will evaluate 2 different self-injection investigational devices: the bimekizumab-SS-1mL and the bimekizumab-AI-1mL. The 2mL device cohort will also evaluate 2 different self-injection investigational devices: the bimekizumab-SS-2mL and the bimekizumab-AI-2ml. The data for each cohort will be analyzed and reported separately.

1mL Device Cohort

Subjects who enroll in the 1mL device cohort of DV0002 will begin the DV0002 substudy and the PS0014 study at the same time, and as such, the Baseline visit and all subsequent study visits (up to Week 16) will be the same.

To compensate for subjects who have different study treatments between the feeder studies and DV0002, the 1mL cohort of the DV0002 substudy is planned to enroll approximately 200 subjects (100 subjects per device arm) to ensure that approximately 50 subjects per device arm are evaluable for steady state trough PK level analyses. 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.

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In the DV0002 substudy 1mL device cohort, 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 by study personnel for safety and effectiveness 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.

2mL Device Cohort

Subjects who participated in the 1mL device cohort are not eligible to participate in the 2mL device cohort. 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 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.

In the DV0002 substudy, for the 2ml devices, the 320mg bimekizumab dose will be self-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 #2

Section 2 Introduction, paragraph 3 and 4

The DV0002 study is a substudy of the PS0014 study. 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 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. Full descriptions of the 2 devices are provided in Section 7.1.1 and Section 7.1.2, respectively.

The proposed study is planned to demonstrate that adult subjects with moderate to severe chronic plaque PSO can safely and effectively self-inject bimekizumab using the bimekizumab-SS-1mL or the bimekizumab-AI-1mL.

Has been changed to:

The DV0002 study is a substudy of the PS0014 study. 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 in a 1mL PFS. The DV0002 substudy will evaluate ~~2~~**4** self-injection investigational devices: the ~~1mL~~ bimekizumab-SS-1mL ~~and~~, the ~~1mL~~ bimekizumab-AI-1mL, **the bimekizumab-SS-2mL, and the bimekizumab-AI-2ml**. Full descriptions of the ~~2~~**4** devices are provided in Section 7.1.1, Section 7.1.2, **Section 7.1.3 and Section 7.1.4,** respectively.

The proposed ~~study~~**substudy** is planned to demonstrate that adult subjects with moderate to severe chronic plaque PSO can safely and effectively self-inject bimekizumab using the

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bimekizumab-SS-1mL ~~or the,~~ bimikizumab-AI-1mL, **bimekizumab-SS-2mL, or bimekizumab-AI-2mL device**.

For subjects in the 1mL device cohort, 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. Subjects who participated in the 1mL device cohort of DV0002 are not eligible to enroll in the 2mL device cohort.

Once the 1mL device cohort has finished enrolling, the 2mL device cohort will start enrolling. Subjects in this cohort will be randomly assigned in a 1:1 ratio to perform self-injection using either the bimekizumab-SS-2mL or bimekizumab-AI-2mL device.

Change #3

Section 3.1 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 3.2 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 3.3 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).

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- 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 4.1.1 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

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- 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 4.1.2 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 4.1.1).

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 4.1.1).

Change #8

Section 4.1.3.1 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 9.1).
- 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

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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 9.1).
- 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 4.1.3.2 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 5.1 Study description, paragraph 1 through the paragraph immediately following Table 5-1

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, and 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 or the bimekizumab-AI-1mL for the sc self-injection of bimekizumab solution by subjects with PSO will be evaluated.

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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 instructions for use (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).

During the 16-week Treatment Period of DV0002, subjects will receive either bimekizumab 320mg Q8W or bimekizumab 320mg Q4W, based on their assigned dosing at Baseline (Table 5-1). Baseline for DV0002 and Baseline for PS0014 will occur at the same time, and the same interactive response technology (IRT) will be used for both studies. The 320mg bimekizumab dose will be administered as two 160mg injections, and both injections will be either self-administered using the test device (at Baseline and Week 8) or administered by study personnel using the 1mL PFS (at Week 4 and Week 12 for subjects in the Q4W dosing arm and at Week 16 for both dosing arms). This dose regimen will remain stable for the entire 16-week Treatment Period of DV0002, as per PS0014 design. The DV0002 substudy will evaluate 2 self-injection investigational devices: the bimekizumab-SS-1mL and the bimekizumab-AI-1mL.

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 (see Section 7.10). 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).

Table 5-1: Bimekizumab administration schedule

Dose Regimen	Baseline	Week 4	Week 8	Week 12	Week 16
320mg Q8W	S	NA	S	NA	SP
320mg Q4W	S	SP	S	SP	SP

bimekizumab-AI-1mL=1mL bimekizumab auto-injector; bimekizumab-SS-1mL=1mL bimekizumab safety syringe; NA=not applicable; Q4W=every 4 weeks; Q8W=every 8 weeks; S=subject performing self-injection using the test device; SP=study personnel performing injection using the 1mL pre-filled syringe

Note: For S injections, the 320mg bimekizumab dose will be administered as two 160mg injections (using 2 bimekizumab-SS-1mL or 2 bimekizumab-AI-1mL). For SP injections, the 320mg bimekizumab dose will be administered as two 160mg injections (using prefilled syringes). Both injections will be administered in the same manner (eg, both self-administered injections or both study personnel-administered injections), but each injection will be administered at a separate injection site and rotation between injection sites should be observed.

Note: Visits in the DV0002 substudy correlate with the same visit in the PS0014 study (ie, the DV0002 Baseline Visit is the PS0014 Baseline Visit). Dose regimen will be assigned at Baseline, and the same interactive response technology will be used for both studies

The bimekizumab administration schedule optimizes the collection of PK trough data within the constraints of a short treatment period and a Q4W and Q8W dosing regimen. At Weeks 4 and 12, subjects on the Q4W dosing regimen will be injected by study personnel with two injections each of 160 mg bimekizumab using a 1mL PFS (i.e., the same device as that used in PS0014).

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For these subjects, the Q4W administration schedule will provide PK trough data associated with injection by:

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, and 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 solution 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 instructions for use (IFU) and any other applicable training materials.

1mL Device Cohort

For the 1mL device cohort, 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).

During the 16-week Treatment Period of DV0002, subjects will receive either bimekizumab 320mg Q8W or bimekizumab 320mg Q4W, based on their assigned dosing at Baseline (Table 5-1). Baseline for DV0002 and Baseline for PS0014 will occur at the same time, and the same interactive response technology (IRT) will be used for both studies. The 320mg bimekizumab dose will be administered as two 160mg injections, and both injections will be either self-administered using the ~~test~~**investigational** device (at Baseline and Week 8) or administered by study personnel using the 1mL PFS (at Week 4 and Week 12 for subjects in the Q4W dosing arm and at Week 16 for both dosing arms). This dose regimen will remain stable for the entire 16-week Treatment Period of DV0002, as per PS0014 design. The DV0002 substudy will evaluate 2 self-injection investigational devices: the bimekizumab-SS-1mL and the bimekizumab-AI-1mL.

Eligible subjects **(PS0014 entry criteria and Section 6 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 (see Section 7.10). 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).

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Table 5-1: Bimekizumab administration schedule **visits in DV0002 substudy 1mL device cohort**

Dose Regimen	Baseline	Week 4	Week 8	Week 12	Week 16
320mg Q8W	S	NA	S	NA	SP
320mg Q4W	S	SP	S	SP	SP

bimekizumab-AI-1mL=1mL bimekizumab auto-injector; bimekizumab-SS-1mL=1mL bimekizumab safety syringe; NA=not applicable; Q4W=every 4 weeks; Q8W=every 8 weeks; S=subject performing self-injection using the ~~test~~ **investigational** device; SP=study personnel performing injection using the 1mL pre-filled syringe

Note: For S injections, the 320mg bimekizumab dose will be administered as two 160mg injections (using 2 bimekizumab-SS-1mL or 2 bimekizumab-AI-1mL). For SP injections, the 320mg bimekizumab dose will be administered as two 160mg injections (using prefilled syringes). Both injections will be administered in the same manner (eg, both self-administered injections or both study personnel-administered injections), but each injection will be administered at a separate injection site and rotation between injection sites should be observed.

Note: **For the 1mL cohort, v**isits in the DV0002 substudy correlate with the same visit in the PS0014 study (ie, the DV0002 Baseline Visit is the PS0014 Baseline Visit). Dose regimen will be assigned at Baseline, and the same interactive response technology will be used for both studies.

The bimekizumab administration schedule optimizes the collection of PK trough data within the constraints of a short treatment period and a Q4W and Q8W dosing regimen. At Weeks 4~~, and~~ 12, **and 16,** subjects on the Q4W dosing regimen will be injected by study personnel with ~~two~~ **2** injections each of 160mg bimekizumab using a 1mL PFS (~~i.e.~~**ie**, the same device as that used in PS0014). For these subjects, the Q4W administration schedule will provide PK trough data associated with injection by:

Change #11
Section 5.1 Study description, Addition of 2mL device cohort

The following text was added at the end of Section 5.1 and appears before Section 5.1.1:

2mL Device Cohort

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.

During the Treatment Period of DV0002, subjects will receive either bimekizumab 320mg Q8W or bimekizumab 320mg Q4W, based on their assigned dosing at Baseline of PS0014 (Table 5-3). 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. The same IRT will be used for both studies. The 320mg bimekizumab dose will either be self-administered as 1 injection using the assigned investigational device (at DV0002 Baseline and Week 8) or administered as 2 injections by study personnel using the 1mL PFS (at DV0002 Week 4 and Week 12 for subjects in the Q4W dosing arm and at DV0002 Week 16

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for both dosing arms). This dose regimen will remain stable for the entire 16-week Treatment Period of DV0002, per the PS0014 design.

Eligible subjects (PS0014 entry criteria and Section 6 DV0002 entry criteria) who have not participated in the 1mL device cohort, will be randomly assigned in a 1:1 ratio to perform self-injection using either the bimekizumab-SS-2mL or the bimekizumab-AI-2mL (see Section 7.10). Regardless of the assigned dose regimen, subjects will perform self-injection with the assigned devices only at DV0002 Baseline and at DV0002 Week 8.

Table 5-2: Bimekizumab administration schedule visits in DV0002 substudy 2mL device cohort

	DV0002 Visits				
Dose Regimen	**Baseline**	**Week 4**	**Week 8**	**Week 12**	**Week 16**
320mg Q8W	**S**	**NA**	**S**	**NA**	**SP**
320mg Q4W	**S**	**SP**	**S**	**SP**	**SP**

bimekizumab-AI-2mL=2mL bimekizumab auto-injector; bimekizumab-SS-2mL=2mL bimekizumab safety syringe; IRT = interactive response technology; NA=not applicable; Q4W=every 4 weeks; Q8W=every 8 weeks; S=subject performing self-injection using the investigational device, SP=study personnel performing injection using the 1mL prefilled syringe

Note: For S injections, the 320mg bimekizumab dose will be administered as a single injection (using the bimekizumab-SS-2mL or bimekizumab-AI-2mL devices). For SP injections, the 320mg bimekizumab dose will be administered as two 160mg injections (using 2 prefilled syringes). The injections will be administered in the same manner (eg, both self-administered injections or both SP-administered injections), but each injection will be administered at a separate injection site and rotation between injection sites should be observed.

Note: For the 2mL device cohort, Baseline for DV0002 will occur at PS0014 Week 24, Week 28, or Week 32 for subjects receiving bimekizumab Q4W, or at PS0014 Week 24 or Week 32 for subjects receiving bimekizumab Q8W. Dose regimen will be assigned at Baseline of the PS0014 study, and the same IRT will be used for both the PS0014 and DV0002 studies.

The bimekizumab administration schedule optimizes the collection of PK trough data within the constraints of a short treatment period and a Q4W and Q8W dosing regimen. At Weeks 4, 12, and 16, subjects on the Q4W dosing regimen will be injected by study personnel with 2 injections each of 160 mg bimekizumab using a 1mL PFS (ie, the same device as that used in PS0014). For these subjects, the Q4W administration schedule will provide PK trough data associated with injection by:

- ***Study personnel using the 1mL PFS*** **from PK samples collected (before self-injection) at DV0002 Baseline and Week 8 (ie, PK data from 2 timepoints)**
- ***Subject self-injection using the assigned device*** **from PK samples collected (before injection by study personnel) at Week 4 and Week 12 (ie, PK data from 2 timepoints)**

At DV0002 Baseline and Week 8, subjects on the Q8W dosing regimen will self-inject 1 injection using the assigned 2mL device (bimekizumab-SS-2mL or the 1 bimekizumab-AI-

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2mL). For these subjects, the Q8W administration schedule will provide PK trough data associated with injection by:

- ***Study personnel using the 1mL PFS*** **from PK samples collected (before self-injection) at DV0002 Baseline (ie, PK data from 1 timepoint)**
- ***Subject self-injection using the assigned device*** **from PK samples collected (before self-injection) at DV0002 Week 8 and (before injection by study personnel) at DV0002 Week 16 (ie, PK data from 2 timepoints)**

In addition to self-injections, DV0002 substudy-specific assessments (eg, study personnel evaluation, SIAQ responses, VAS for injection site pain, and PK analyses; see Section 5.2) will be performed from DV0002 Baseline through Week 16 (inclusive). An SFU telephone call will occur 1 week after the last self-administration (at DV0002 Week 9).

After Week 16 in the DV0002 substudy, subjects will continue in PS0014. Studies DV0002 and PS0014 will share a common database/eCRF system (including common AE reporting) and a common IRT.

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 (see Section 6.3). Subjects who are withdrawn from bimekizumab treatment (PS0014 study) during the course of DV0002 will also be required to follow the PS0014 withdrawal procedures.

Change #12

Section 5.1.2 Planned number of subjects and sites

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 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 5.2 Schedule of study assessments

The schedule of assessments in presented in Table 5-2 and includes assessments performed specifically in the DV0002 substudy and assessments performed as part of the PS0014 study. Assessments specific to the DV0002 substudy are labeled for clarity.

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Table 5-2: Schedule of study assessments

Visit [a] / Week / Procedures	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (Device SFU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16
Informed consent for DV0002 and PS0014 assessments	X					
Inclusion/exclusion	X					
Physical exam [b, c]	X				X	
Body weight	X					
Vital signs [d]	X	X	X			X
Hematology and chemistry	X	X	X			X
Urinalysis	X	X	X			X
Urine drug screen	X					
ECG	X					
Pregnancy testing [e]	X	X	X		X	X
TB questionnaire	X				X	
Blood sample for bimekizumab plasma concentrations [f] (DV0002-specific for Weeks 4, 8, and 12)	X	X [g]	X		X [g]	X [h]
Blood sample for anti-bimekizumab antibodies [f]	X					X
PASI	X	X	X		X	X
Percentage of BSA	X	X	X		X	X
IGA	X	X	X		X	X

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Table 5-2: Schedule of study assessments

Visit [a] / Week / Procedures	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (Device SPU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16
DLQI	X					
PHQ-9	X	X	X			X
eC-SSRS	X	X	X			X
mNAPSI [i]	X					
Scalp IGA [j]	X					
pp-IGA [k]	X					
EQ-5D-3L	X					
SF-36	X					
PGA of PSO	X					
PASE	X					
PGADA [l]	X					
WPAI-SHP v2.0	X					
Concomitant medication (DV0002-specific for Week 9)	X	X	X	X	X	X
Adverse events [m] (DV0002-specific for Week 9)	X	X	X	X	X	X
Random assignment to device (DV0002-specific)	X					
IRT contact	X	X	X		X	X

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Table 5-2: Schedule of study assessments

Visit [a] / Week / Procedures	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (Device SPU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16
Subject training for VAS and SIAQ Questionnaire (DV0002-specific)	X					
Pre-injection SIAQ Questionnaire [n] (DV0002-specific)	X					
Subject training for self-injection (DV0002-specific)	X					
Bimekizumab administration by study personnel using the PFS [o]		X [g]			X [g]	X
Subject self-injection of bimekizumab using the assigned device [p] (DV0002-specific)	X		X			
Study personnel evaluation of self-injection (DV0002-specific)	X		X			
Study personnel evaluation of post-use device for structural/mechanical integrity (DV0002-specific)	X		X			
VAS for injection site pain (DV0002-specific)	X		X			
Post-injection SIAQ Questionnaire [n] (DV0002-specific)	X		X			
Drug and device accountability (DV0002-specific)	X	X	X		X	X

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Table 5-2: Schedule of study assessments

Procedures \ Visit [a] Week	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (Device SFU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16

bimekizumab-AI-1mL=1mL bimekizumab auto-injector; bimekizumab-SS-1mL=1mL bimekizumab safety syringe; BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; PASI=Psoriasis Area Severity Index; PGA=Patient Global Assessment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire 9; pp-IGA=palmoplantar Investigator's Global Assessment; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; SF-36=Short Form 36-item Health Survey; SFU=safety follow-up; SIAQ=Self-injection Assessment Questionnaire; TB=tuberculosis; VAS=visual analog scale; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

[a] Visit windows of ±7 days from the first dose at all visits except Visit 3a (SFU telephone call). The SFU telephone call window is 7 days from the last dose in the DV0002 substudy, ±3 days.

[b] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.

[c] The physical exam will include examination of the following systems: eyes, hair, and skin; respiratory; cardiovascular; and gastrointestinal.

[d] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.

[e] Pregnancy testing will consist of urine pregnancy tests at all visits. Pregnancy test results must be negative prior to administering investigational medicinal product.

[f] All blood samples will be taken prior to dosing.

[g] This will only be done for subjects who receive bimekizumab Q4W.

[h] This will only be done for subjects who receive bimekizumab Q8W.

[i] The mNAPSI will be assessed only in subjects with nail involvement at Baseline in the feeder studies.

[j] The scalp IGA will only be assessed for those subjects with scalp involvement (scalp IGA score >0) at Baseline in the feeder studies.

[k] The pp-IGA will only be assessed in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline in the feeder studies.

[l] The PGADA is assessed only for subjects with psoriatic arthritis at Baseline in the feeder studies.

[m] Adverse events not related to the investigational devices will be reported in PS0014 and adverse device effects and device deficiencies will be reported in DV0002. A single safety database will be used for both studies.

[n] Version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL, while version 2.1 will be used to assess bimekizumab-AI-1mL (see Section 9.1).

[o] The dosing window is ±7 days relative to the scheduled dosing visit.

[p] The 320mg bimekizumab dose will be administered as two 160mg injections (using 2 bimekizumab-SS-1mL devices or 2 bimekizumab-AI-1mL devices).

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Has been changed to:

The schedule of assessments in presented in ~~Table 5-2~~ **Table 5-3 for the 1mL device cohort. For subjects in the 1mL device cohort, Baseline for DV0002 corresponds to Baseline in PS0014, and the subsequent study visits are the same in both studies.** ~~Table 5-2~~ **Table 5-3** includes assessments performed specifically in the DV0002 substudy and assessments performed as part of the PS0014 study**, inclusive**. Assessments specific to the DV0002 substudy are labeled for clarity.

For subjects in the 2mL device cohort, Baseline for DV0002 can correspond to the PS0014 Week 24, Week 28, or Week 32 visits for subjects receiving bimekizumab Q4W and to the PS0014 Week 24 or Week 32 visits for subjects receiving bimekizumab Q8W. The schedule of assessments for the PS0014 Week 24 through Week 48 visits is presented in Table 5-4. The additional assessments to be performed for the DV0002 substudy in the 2mL device cohort specifically are presented in Table 5-5.

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Table 5-3: Schedule of ~~study~~ assessments **for the PS0014 study and DV0002 substudy (1mL device cohort)**

Visit [a] / Week / Procedures	**DV0002 Treatment Period**					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (**DV0002** SFU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16
Informed consent for DV0002 and PS0014 assessments	X					
Inclusion/exclusion	X					
Physical exam [b, c]	X				X	
Body weight	X					
Vital signs [d]	X	X	X			X
Hematology and chemistry	X	X	X			X
Urinalysis	X	X	X			X
Urine drug screen	X					
ECG	X					
Pregnancy testing [e]	X	X	X		X	X
TB questionnaire	X				X	
Blood sample for bimekizumab plasma concentrations [f] (DV0002-specific for Weeks 4, 8, and 12)	X	X [g]	X		X [g]	X [h]
Blood sample for anti-bimekizumab antibodies [f]	X					X
PASI	X	X	X		X	X
Percentage of BSA	X	X	X		X	X

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Table 5-3: Schedule of ~~study~~ assessments **for the PS0014 study and DV0002 substudy (1mL device cohort)**

Visit [a] / Week / Procedures	**DV0002 Treatment Period**					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (**DV0002** SFU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16
IGA	X	X	X		X	X
DLQI	X					
PHQ-9	X	X	X			X
eC-SSRS	X	X	X			X
mNAPSI [i]	X					
Scalp IGA [j]	X					
pp-IGA [k]	X					
EQ-5D-3L	X					
SF-36	X					
PGA of PSO	X					
PASE	X					
PGADA [l]	X					
WPAI-SHP v2.0	X					
Concomitant medication (DV0002-specific for Week 9)	X	X	X	X	X	X
Adverse events [m] (DV0002-specific for Week 9)	X	X	X	X	X	X

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Table 5-3: Schedule of ~~study~~ assessments **for the PS0014 study and DV0002 substudy (1mL device cohort)**

Procedures \ Visit [a] Week	**DV0002 Treatment Period**					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (**DV0002** SFU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16
Random assignment to device (DV0002-specific)	X					
IRT contact	X	X	X		X	X
Subject training for VAS and SIAQ Questionnaire (DV0002-specific)	X					
Pre-injection SIAQ Questionnaire [n] (DV0002-specific)	X					
Subject training for self-injection (DV0002-specific)	X					
Bimekizumab administration by study personnel using the PFS [o]		X [g]			X [g]	X
Subject self-injection of bimekizumab using the assigned device [o, p] (DV0002-specific)	X		X			
Study personnel evaluation of self-injection (DV0002-specific)	X		X			
Study personnel evaluation of post-use device for structural/mechanical integrity (DV0002-specific)	X		X			

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Table 5-3: Schedule of ~~study~~ assessments **for the PS0014 study and DV0002 substudy (1mL device cohort)**

Procedures \ Visit [a] Week	**DV0002 Treatment Period**					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (**DV0002** SFU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16
VAS for injection site pain (DV0002-specific)	X		X			
Post-injection SIAQ Questionnaire [n] (DV0002-specific)	X		X			
Drug and device accountability (DV0002-specific)	X	X[g]	X		X[g]	X

bimekizumab-AI-1mL=1mL bimekizumab auto-injector; bimekizumab-SS-1mL=1mL bimekizumab safety syringe; BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; PASI=Psoriasis Area Severity Index; PGA=Patient Global Assessment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire 9; pp-IGA=palmoplantar Investigator's Global Assessment; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; SF-36=Short Form 36-item Health Survey; SFU=safety follow-up; SIAQ=Self-injection Assessment Questionnaire; TB=tuberculosis; VAS=visual analog scale; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

[a] Visit windows of ±7 days from the first dose at all visits except Visit 3a (SFU telephone call). The SFU telephone call window is 7 days from the last dose in the DV0002 substudy, ±3 days.

[b] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.

[c] The physical exam will include examination of the following systems: eyes, hair, and skin; respiratory; cardiovascular; and gastrointestinal.

[d] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.

[e] Pregnancy testing will consist of urine pregnancy tests at all visits. Pregnancy test results must be negative prior to administering investigational medicinal product.

[f] All blood samples will be taken prior to dosing.

[g] This will only be done for subjects who receive bimekizumab Q4W.

[h] This will only be done for subjects who receive bimekizumab Q8W.

[i] The mNAPSI will be assessed only in subjects with nail involvement at Baseline in the feeder studies.

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Table 5-3: Schedule of ~~study~~ assessments **for the PS0014 study and DV0002 substudy (1mL device cohort)**

Procedures \ Visit [a] Week	**DV0002 Treatment Period**					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (**DV0002** SFU)	Visit 4	Visit 5
	Baseline/Feeder Study Final Visit	Week 4	Week 8	Week 9	Week 12	Week 16

[j] The scalp IGA will only be assessed for those subjects with scalp involvement (scalp IGA score >0) at Baseline in the feeder studies.
[k] The pp-IGA will only be assessed in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline in the feeder studies.
[l] The PGADA is assessed only for subjects with psoriatic arthritis at Baseline in the feeder studies.
[m] Adverse events not related to the investigational devices will be reported in PS0014 and adverse device effects and device deficiencies will be reported in DV0002. A single safety database will be used for both studies.
[n] Version 2.0 of the SIAQ will be used to assess bimekizumab-SS-1mL, while version 2.1 will be used to assess bimekizumab-AI-1mL (see Section 9.1).
[o] The dosing window is ±7 days relative to the scheduled dosing visit.
[p] The 320mg bimekizumab dose will be administered as two 160mg injections (using 2 bimekizumab-SS-1mL devices or 2 bimekizumab-AI-1mL devices).

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Table 5-4: Schedule of assessments for the PS0014 study (2mL device cohort)

Procedures \ Week	Week 24[a]	Week 28[a]	Week 32[a]	Week 36	Week 40	Week 44	Week 48
Physical exam[b,c]	X			X			X
Body weight							X
Vital signs[d]	X		X		X		X
Hematology and chemistry	X		X		X		X
Urinalysis	X		X		X		X
ECG							X
Pregnancy testing[e]	X	X	X	X	X	X	X
IGRA TB test							X
TB questionnaire	X			X			X
Blood sample for bimekizumab plasma concentrations[f]	X				X		X
Blood sample for anti-bimekizumab antibodies[f]	X				X		X
PASI	X	X	X	X	X	X	X
Percentage of BSA	X	X	X	X	X	X	X
IGA	X	X	X	X	X	X	X
DLQI	X						X
PHQ-9	X		X		X		X
eC-SSRS	X		X		X		X
mNAPSI[g]	X						X
Scalp IGA[h]	X						X

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Table 5-4: Schedule of assessments for the PS0014 study (2mL device cohort)

Procedures \ Week	Week 24[a]	Week 28[a]	Week 32[a]	Week 36	Week 40	Week 44	Week 48
pp-IGA[i]	X						X
EQ-5D-3L	X						X
SF-36	X						X
PGA of PSO	X						X
PASE[j]							X
PGADA[j]	X						X
WPAI-SHP V2.0	X						X
TSQM-9							X
Concomitant medication	X	X	X	X	X	X	X
Adverse events	X	X	X	X	X	X	X
IRT	X	X	X	X	X	X	X
Bimekizumab administration[k,l]	X	X	X	X	X	X	X
Subject training on home self-injection[m]					X	X	

BSA=body surface area; DLQI=Dermatology Life Quality Index; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IMP=investigational medicinal product; IRT=interactive response technology; mNAPSI=modified Nail Psoriasis Severity Index; PASE=Psoriatic Arthritis Screening and Evaluation; PASI=Psoriasis Area Severity Index; PGA=Patient Global Assessment; PGADA=Patient's Global Assessment of Disease Activity; PHQ-9=Patient Health Questionnaire-9; pp-IGA=palmoplantar Investigator's Global Assessment; PsA=psoriatic arthritis; PSO=psoriasis; Q4W=every 4 weeks; Q8W=every 8 weeks; SF-36=Short Form 36-item Health Survey; TB=tuberculosis; TSQM-9=Treatment Satisfaction Questionnaire for Medication; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

Note: Starting at Week 48 of the PS0014 Treatment Period, subjects may self-inject IMP at home; self-injection training will be provided to the subject/caregivers by qualified site personnel (refer to PS0014 protocol).

[a] For the 2mL device cohort, Baseline of DV0002 can occur at PS0014 Week 24, Week 28, or Week 32 for subjects receiving bimekizumab Q4W and at PS0014 Week 24 or Week 32 for subjects receiving bimekizumab Q8W.

[b] Includes evaluation of signs and symptoms of active TB and risk for exposure to TB.

[c] The physical examination will be performed as per the PS0014 protocol Section 9.3.5.

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Table 5-4: Schedule of assessments for the PS0014 study (2mL device cohort)

Procedures \ Week	Week 24[a]	Week 28[a]	Week 32[a]	Week 36	Week 40	Week 44	Week 48

[d] Vital signs (sitting systolic and diastolic blood pressure, pulse rate, and temperature) are to be measured prior to blood sampling, and prior to dosing, where applicable.
[e] Urine pregnancy testing will be performed at all visits. Pregnancy test results must be negative prior to administering IMP.
[f] All blood samples taken prior to dosing.
[g] The mNAPSI will be assessed only in subjects with nail involvement at Baseline in the feeder studies.
[h] The scalp IGA will only be assessed for those subjects with scalp involvement (scalp IGA score >0) at Baseline in the feeder studies.
[i] The pp-IGA will only be assessed in subjects with palmoplantar involvement (pp-IGA score >0) at Baseline in the feeder studies
[j] The PGADA and the PASE are assessed only for subjects with PsA at Baseline in the feeder studies.
[k] The dosing window is ±7 days relative to the scheduled dosing visit.
[l] Only subjects receiving IMP Q4W are dosed on Week 28, Week 36, and Week 44.
[m] Subject training on at-home self-injection is to be performed as described in the PS0014 protocol Section 7.2. Starting at Week 48 of the PS0014 Treatment Period, subjects may self-inject IMP at home.

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Table 5-5: Schedule of assessments for the DV0002 substudy (2mL device cohort)

Procedures / Visit [a] / Week	DV0002 Treatment Period					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (Device SFU)	Visit 4	Visit 5
	Baseline[b]	Baseline + 4 weeks	Baseline + 8 weeks	Baseline + 9 weeks	Baseline + 12 weeks	Baseline + 16 weeks
Informed consent for DV0002	X					
Random assignment to device (DV0002-specific)	X					
IRT contact	X	X	X		X	X
Blood sample for bimekizumab plasma concentrations[c] (DV0002-specific for Weeks 4, 8, and 12)	X	X[d]	X		X[d]	X[e]
Subject training for VAS and SIAQ Questionnaire (DV0002-specific)	X					
Pre-injection SIAQ Questionnaire[f] (DV0002-specific)	X					
Subject training for self-injection (DV0002-specific)	X					
Bimekizumab administration by study personnel using the PFS[g]		X[d]			X[d]	X
Subject self-injection of bimekizumab using the assigned device[g,h] (DV0002-specific)	X		X			
Study personnel evaluation of self-injection (DV0002-specific)	X		X			

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Table 5-5: Schedule of assessments for the DV0002 substudy (2mL device cohort)

Procedures / Visit [a] Week	DV0002 Treatment Period					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (Device SFU)	Visit 4	Visit 5
	Baseline[b]	Baseline + 4 weeks	Baseline + 8 weeks	Baseline + 9 weeks	Baseline + 12 weeks	Baseline + 16 weeks
VAS for injection site pain (DV0002-specific)	X		X			
Post-injection SIAQ Questionnaire[f] (DV0002-specific)	X		X			
Study personnel evaluation of post-use device for structural/mechanical integrity (DV0002-specific)	X		X			
Drug and device accountability (DV0002-specific)	X	X[d]	X		X[d]	X
Concomitant medication				X		
Adverse Events[i]				X		

IRT=interactive response technology; Q4W=every 4 weeks; Q8W=every 8 weeks; SFU=safety follow-up; SIAQ=Self-injection Assessment Questionnaire; VAS=visual analog scale

[a] Visit windows of ±7 days from the first dose at all visits except Visit 3a (SFU telephone call). The SFU telephone call window is 7 days from the last dose in the DV0002 substudy, ±3 days.

[b] For subjects in the 2mL device cohort, Baseline for DV0002 corresponds to PS0014 Week 24, Week 28, or Week 32 for subjects receiving bimekizumab Q4W and to PS0014 Week 24 or Week 32 for subjects receiving bimekizumab Q8W. Refer to Table 5-4 for PS0014 study assessments.

[c] All blood samples will be taken prior to dosing. For detail on PK sampling in the 2mL device cohort, refer to Table 10-1 in Section 10.

[d] This will only be done for subjects who receive bimekizumab Q4W.

[e] This will only be done for subjects who receive bimekizumab Q8W.

[f] Version 2.0 of the SIAQ will be used to assess bimekizumab-SS-2mL, while version 2.1 will be used to assess bimekizumab-AI-2mL (see Section 9.1).

[g] The dosing window is ±7 days relative to the scheduled dosing visit.

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Table 5-5: Schedule of assessments for the DV0002 substudy (2mL device cohort)

Visit [a] / Week / Procedures	DV0002 Treatment Period					
	Visit 1	Visit 2	Visit 3	Visit 3a Telephone Call (Device SFU)	Visit 4	Visit 5
	Baseline[b]	Baseline + 4 weeks	Baseline + 8 weeks	Baseline + 9 weeks	Baseline + 12 weeks	Baseline + 16 weeks

[h] The 320mg bimekizumab dose will be administered as 1 injection using the bimekizumab-SS-2mL device or bimekizumab-AI-2mL device.
[i] Adverse events not related to the devices will be reported in PS0014 and adverse device effects and device deficiencies will be reported in DV0002. A single safety database will be used for both studies.

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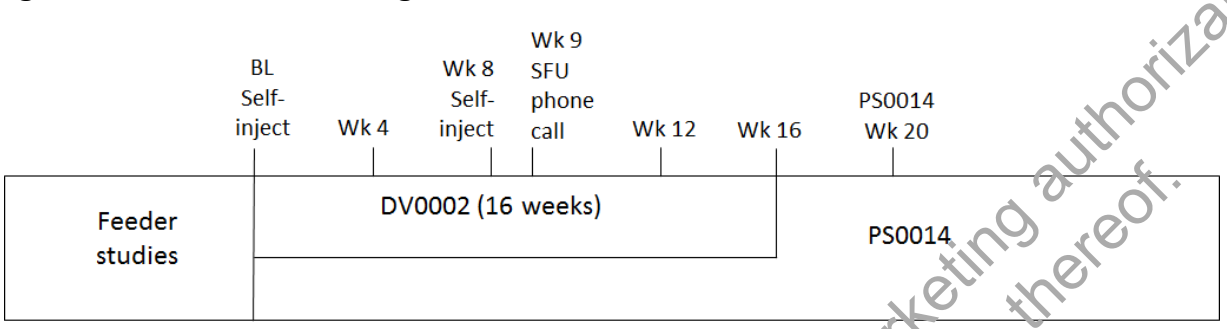
Change #14

Section 5.3 Schematic diagram

The study schematic diagram for DV0002 is presented in Figure 5-1.

Figure 5-1: Schematic diagram

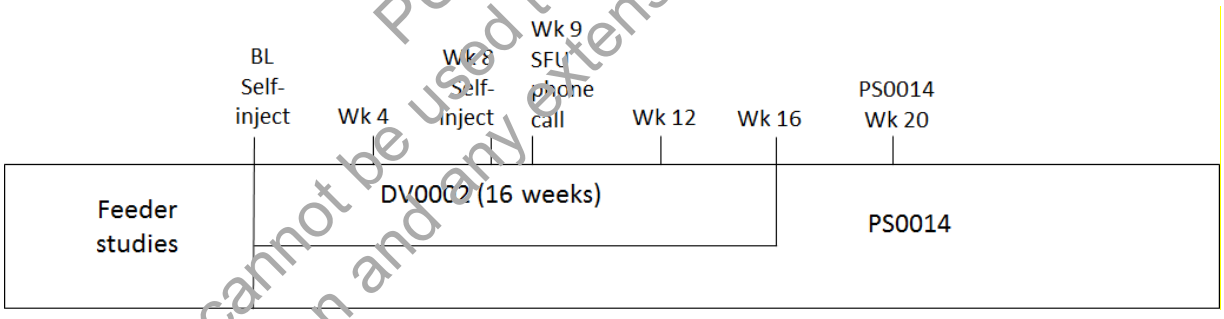


BL=Baseline; Q4W=every 4 weeks; Q8W=every 8 weeks; self-inject=self-injection; SFU=safety follow-up; Wk=week
Note: Phase 3 feeder studies include PS0008, PS0009, and PS0013.
Note: Subjects will receive 320mg bimekizumab either Q4W or Q8W. Bimekizumab will be self-administered only at Baseline and at Week 8 (study personnel will administer bimekizumab at other visits).

Has been changed to:

The study schematic diagram for DV0002 **1 mL device cohort** is presented in Figure 5-1, **and the 2mL device cohort is presented in Figure 5-2.**

Figure 5-1: Schematic diagram **for the 1mL device cohort**



BL=Baseline; Q4W=every 4 weeks; Q8W=every 8 weeks; self-inject=self-injection; SFU=safety follow-up; Wk=week
Note: Phase 3 feeder studies include PS0008, PS0009, and PS0013.
Note: Subjects will receive 320mg bimekizumab either Q4W or Q8W. Bimekizumab will be self-administered only at Baseline and at Week 8 (study personnel will administer bimekizumab at other visits**, as applicable**).
Note: For the 1mL device cohort, subjects will begin the DV0002 substudy and the PS0014 study at the same time; therefore, Baseline for DV0002 corresponds to Baseline for PS0014.

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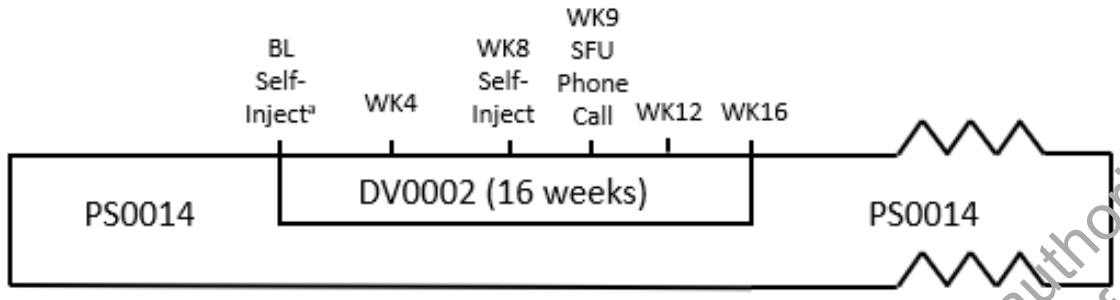
Figure 5-2: Schematic diagram for the 2mL device cohort



BL=Baseline; Q4W=every 4 weeks; Q8W=every 8 weeks; self-inject=self-injection; SFU=safety follow-up; WK=week

Note: Subjects will receive 320mg bimekizumab either Q4W or Q8W. Bimekizumab will be self-administered only at DV0002 Baseline and 8 weeks after training (study personnel will administer bimekizumab at other visits).

[a] For the 2mL device cohort, subjects will not begin the DV0002 substudy and the PS0014 study at the same time. Baseline for DV0002 corresponds to the PS0014 Week 24, Week 28, or Week 32 visit for subjects receiving bimekizumab Q4W and to the PS0014 Week 24 or Week 32 visit for subjects receiving bimekizumab Q8W.

Change #15

Section 5.4 Rationale for study design and selection of dose, paragraph 2

It is expected that most individuals who will use commercial bimekizumab for the treatment of moderate to severe chronic plaque PSO will self-inject bimekizumab and also that these individuals will prefer to have options for the self-administration of their medication. DV0002 will therefore evaluate the safe and effective use of 2 different self-injection investigational devices: bimekizumab-SS-1mL and bimekizumab-AI-1mL. In addition, DV0002 will assess trough PK 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).

Has been changed to:

It is expected that most individuals who will use commercial bimekizumab for the treatment of moderate to severe chronic plaque PSO will self-inject bimekizumab and also that these individuals will prefer to have options for the self-administration of their medication. DV0002 will therefore evaluate the safe and effective use of ~~2~~**4** different self-injection investigational devices **in 2 cohorts: the 1mL device cohort and the 2mL device cohort. The 1mL device cohort will evaluate the** bimekizumab-SS-1mL and bimekizumab-AI-1mL~~.~~ **investigational devices. The 2mL device cohort will evaluate the bimekizumab-SS-2mL and bimekizumab-AI-2mL investigational devices.** In addition, DV0002 will assess trough PK 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).

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Change #16

Section 6.2 Exclusion Criteria

Subjects are not permitted to enroll in DV0002 if any of the PS0014 study exclusion criteria are met.

Has been changed to:

Subjects are not permitted to enroll in DV0002 if any of the PS0014 study exclusion criteria are met. **Subjects who participated in the 1mL device cohort of DV0002 are not eligible to enroll in the 2mL device cohort.**

Change #17

Section 7 Investigational Medicinal Product and Device Presentation

In the DV0002 substudy, the term IMP refers to the bimekizumab drug product. The term investigational device refers to 2 different self-injection investigational devices (bimekizumab-SS-1mL and bimekizumab-AI-1mL) that are comprised of drug product (IMP) associated with a functional secondary packaging.

Has been changed to:

In the DV0006 substudy, the term IMP refers to the bimekizumab drug product. The term investigational device refers to ~~2~~**4** different self-injection investigational devices (bimekizumab-SS-1mL ~~and,~~ bimekizumab-AI-1mL, **bimekizumab-SS-2mL, and bimekizumab-AI-2mL**) that are comprised of drug product (IMP) associated with a functional secondary packaging.

Change #18

New Section 7.1.3Bimekizumab-SS-2mL and Section 7.1.4 Bimekizumab-AI-2mL

7.1.3 Bimekizumab-SS-2mL

The bimekizumab-SS-2mL, shown in Figure 7-3, consists of the primary container (a glass syringe filled with 2mL of bimekizumab drug product) and a safety syringe.

The bimekizumab-SS-2mL is a single-use syringe with a passive safety feature.

Figure 7-3: Bimekizumab-SS-2mL

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7.1.3.1 Instruction for use of bimekizumab-SS-2mL

The bimekizumab-SS-2mL is used to administer a sc injection in either the right or left lateral abdominal wall or the right or left outer thigh without massage. Treatment of the injection site with an anesthetic cream prior to dosing is not permitted.

During the study (at DV0002 Baseline and Week 8), 1 bimekizumab-SS-2mL device will be used to administer a 320mg injection of bimekizumab. To use the bimekizumab-SS-2mL, the rigid needle shield (RNS) is removed, and the plunger rod is fully depressed, which empties the syringe contents through the needle. When the plunger rod reaches its final position the needle safety retraction mechanism is activated, which retracts the sleeve, syringe, and plunger rod and holds the needle safely within the body molding.

Additional instructions for device use, including the injection angle, are provided in the IFU.

7.1.4 Bimekizumab-AI-2mL

The bimekizumab-AI-2mL, shown in Figure 7-4, consists of the primary container (a glass syringe filled with 2mL of bimekizumab drug product) and an auto injector. The bimekizumab-AI-2mL is a single use auto injector with a passive needle stick safety mechanism.

Figure 7-4: Bimekizumab-AI-2mL

bimekizumab-AI-2mL=2mL bimekizumab auto-injector

7.1.4.1 Instruction for use of bimekizumab-AI-2mL

The bimekizumab-AI-2mL is used to administer a sc injection in either the right or left lateral abdominal wall or the right or left outer thigh without massage. Treatment of the injection site with an anesthetic cream prior to dosing is not permitted.

During the study (at DV0002 Baseline and Week 8), 1 bimekizumab-AI-2mL device will be used to administer a 320mg injection of bimekizumab. To use the bimekizumab-AI-2mL, the cap is removed, and the device is depressed on the injection site. The auto injector

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provides needle insertion, dose delivery, and needle protection through an extending and locking shroud. Needle protection is performed by a shroud that will deploy should the auto-injector lose contact with the skin during an injection.

Additional instructions for device use, including the injection angle, are provided in the IFU.

Change #19

Section 7.2 Treatment to be administered

The IMP used in this study is bimekizumab. Bimekizumab will be supplied at a concentration of 160mg/mL (55mM sodium acetate, 220mM glycine, 0.04% polysorbate 80 at pH 5.0) for sc injection in the bimekizumab-SS-1mL or the bimekizumab-AI-1mL.

The IMP will be administered according to the schedule shown in Table 5-1. Subjects will be assigned to the use of 1 device and will receive the following doses of IMP based on their established dosing regimen in PS0014:

- 320mg bimekizumab, Q8W or
- 320mg bimekizumab, Q4W.

Regardless of the assigned dose regimen, subjects will perform self-injection with the assigned device only at Baseline and at Week 8. The 320mg bimekizumab dose will be administered as two 160mg injections with either 2 bimekizumab-SS-1mL or 2 bimekizumab-AI-1mL devices. At all visits except Baseline and Week 8, the 320mg bimekizumab dose will be administered as two 160mg injections in a 1mL PFS by study personnel (ie, the same administration manner and device used in PS0014).

The investigational devices will be used as described in the IFU. Subjects will be observed onsite for 30 minutes after self-injection with bimekizumab for any AEs. Subjects will be asked to contact the designated site personnel in case any AEs occur outside of the site visits. Of note, reported AEs related to IMP will be assessed within PS0014 and reported ADEs and device deficiencies will be assessed within DV0002.

Has been changed to:

The IMP used in this study is bimekizumab. Bimekizumab will be supplied at a concentration of 160mg/mL (55mM sodium acetate, 220mM glycine, 0.04% polysorbate 80 at pH 5.0) for sc injection ~~in the bimekizumab-SS-1mL or the bimekizumab-AI-1mL~~.

1mL Device Cohort

For the 1mL device cohort, IMP will be slupplied in 2 investigational devices: bimekizumab-SS-1mL or the bimekizumab-AI-1mL.

The IMP will be administered according to the schedule shown in Table 5-1. Subjects will be assigned to the use of 1 device and will receive the following doses of IMP based on their established dosing regimen in PS0014:

- 320mg bimekizumab, Q8W or
- 320mg bimekizumab, Q4W.

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Regardless of the assigned dose regimen, subjects will perform self-injection with the assigned device only at Baseline and at Week 8. **For the 1mL device cohort, t**he 320mg bimekizumab dose will be administered as two 160mg injections with either 2 bimekizumab-SS-1mL or 2 bimekizumab-AI-1mL devices. At all visits except Baseline and Week 8, the 320mg bimekizumab dose will be administered as two 160mg injections in a 1mL PFS by study personnel (ie, the same administration manner and device used in PS0014).

The investigational devices will be used as described in the IFU. Subjects will be observed onsite for 30 minutes after self-injection with bimekizumab for any AEs. Subjects will be asked to contact the designated site personnel in case any AEs occur outside of the site visits. Of note, reported AEs related to IMP will be assessed within PS0014 and reported ADEs and device deficiencies will be assessed within DV0002.

2mL Device Cohort

For the 2mL device Cohort, IMP will be supplied in 2 investigational devices. bimekizumab-SS-2mL or bimekizumab-AI-2mL.

The IMP will be administered according to the schedule shown in Table 5-2. Subjects will be assigned to the use of 1 device and will receive the following doses of IMP based on their dosing regimen in PS0014:

- **320mg bimekizumab, Q8W or**
- **320mg bimekizumab, Q4W.**

Regardless of the assigned dose regimen, subjects will perform self-injection with the assigned device only at DV0002 Baseline and 8 weeks after training with the investigational device. For the 2mL device cohort, 320mg bimekizumab dose will be administered as 1 injection with either the bimekizumab-SS-2mL device or the bimekizumab-AI-2mL device. For subjects who receive bimekizumab Q4W, the bimekizumab dose at Week 4 will be administered as two 160mg injections in a 1mL PFS by study personnel (ie, the same administration manner used in PS0014).

The devices will be used as described in the IFU. Subjects will be observed onsite for 30 minutes after self-injection with bimekizumab for any AEs. Subjects will be asked to contact the designated site personnel in case any AEs occur outside of the site visits. Of note, reported AEs related to IMP will be assessed within PS0014 and reported ADEs and device deficiencies will be assessed within DV0002.

Change #20

Section 7.3 Packaging

The site will receive uniquely-numbered investigational devices (bimekizumab-SS-1mL and bimekizumab-AI-1mL) for use in the DV0002 substudy.

Has been changed to:

The site will receive uniquely-numbered investigational devices (bimekizumab-SS-1mL, ~~and~~ bimekizumab-AI-1mL**, bimekizumab-SS-2mL, and bimekizumab-AI-2mL**) for use in the DV0002 substudy.

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Change #21

Section 7.5 Handling and storage requirements, paragraph 1

The investigational device that houses the naked PFS including IMP must be securely stored at 2ºC to 8ºC (ie, in a refrigerator), that is either in a locked room or in the pharmacy. Appropriate storage conditions must be ensured by controlling refrigerator temperature by using either an automated temperature monitoring and recording system or a minimum/maximum thermometer and completing a daily temperature log in accordance with local requirements. If an out-of-range temperature is noted, the Sponsor or designee must be notified so that a determination can be made whether the product should be used or not.

Has been changed to:

The investigational device**s** that house~~s the naked PFS including~~ IMP must be securely stored at 2ºC to 8ºC (ie, in a refrigerator), that is either in a locked room or in the pharmacy. Appropriate storage conditions must be ensured by controlling refrigerator temperature by using either an automated temperature monitoring and recording system or a minimum/maximum thermometer and completing a daily temperature log in accordance with local requirements. If an out-of-range temperature is noted, the Sponsor or designee must be notified so that a determination can be made whether the product should be used or not.

Change #22

Section 7.7 Procedures for monitoring subject 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.

Has been changed to:

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~~. **Subject compliance will be reported in the PS0014 study.**

Change #23

Section 7.10 Randomization and numbering of subjects, paragraphs 2 and 3

The IRT will generate individual assignments for the self-injection investigational devices. Eligible subjects will be assigned to the investigational devices based on a predetermined production randomization and/or packaging schedule provided by UCB (or designee). All eligible subjects will be randomly assigned to perform self-injection using either the bimekizumab-SS-1mL or the bimekizumab-AI-1mL at a 1:1 ratio. The IRT will allocate kit numbers to the subject based on the subject number during the study.

Subject numbers and kit numbers will be tracked via the IRT.

Has been changed to:

The IRT will generate individual assignments for the self-injection investigational devices. Eligible subjects will be assigned to the investigational devices based on a predetermined

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production randomization and/or packaging schedule provided by UCB (or designee). **In the 1mL device cohort,** all eligible subjects will be randomly assigned to perform self-injection using either the bimekizumab-SS-1mL or the bimekizumab-AI-1mL at a 1:1 ratio. The IRT will allocate kit numbers to the subject based on the subject number during the study.

Once the 1mL device cohort has finished enrolling, the 2mL device cohort will start enrolling. Eligible subjects in the 2mL cohort will be randomly assigned to perform self-injection using either the bimekizumab-SS-2mL or bimekizumab-AI-2mL device at a 1:1 ratio. The IRT will allocate kit numbers to the subject based on the subject number during the study.

Subject numbers and kit numbers will be tracked via the IRT.

Change #24

Section 8 Study Procedures by Visit, paragraph 1

A general overview of the study assessments is provided in Table 5-2. Although Table 5-2 contains assessments for both DV0002 and PS0014, it also indicates which assessments are specific to the DV0002 substudy. Of note, DV0002 and PS0014 will share a common database/eCRF system (including common AE reporting) and a common IRT. The list of procedures at each study visit is described in the following sections.

Has been changed to:

A general overview of the study assessments **for the DV0002 substudy 1mL device cohort** is provided in ~~Table 5-2~~ **Table 5-3**. Although ~~Table 5-2~~**Table 5-3** contains assessments for both DV0002 and PS0014, it also indicates which assessments are specific to the DV0002 substudy. ~~Of note, DV0002 and PS0014 will share a common database/eCRF system (including common AE reporting) and a common IRT.~~ The lists of procedures at each study visit ~~is~~**for the 1mL device cohort are** described in **Section 8.1**~~the following sections~~.

For subjects in the 2mL device cohort, Baseline for DV0002 can correspond to the PS0014 Week 24, Week 28, or Week 32 visits for subjects receiving bimekizumab Q4W or to the PS0014 Week 14 or Week 32 visits for subjects receiving bimekizumab Q8W. For the 2mL device cohort, the schedule of assessments for PS0014 is presented in Table 5-4. The additional assessments to be performed for the DV0002 substudy specifically are presented in Table 5-5 and the list of procedures at each study visit is described in Section 8.2.

Of note, DV0002 and PS0014 will share a common database/eCRF system (including common AE reporting) and a common IRT.

Change #25

Section 8.1 Treatment Period

8.1 Treatment Period

The DV0002 substudy will include all PS0014 study assessments from Baseline to Week 16 (inclusive).

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Has been changed to:

8.1 Treatment Period **for the 1mL Device Cohort**

The DV0002 substudy will include all PS0014 study assessments from Baseline to Week 16 (inclusive). **For subjects in the 1mL device cohort, Baseline for DV0002 corresponds to Baseline in PS0014.**

Change #26

Section 8.1.1 Visit 1 (Baseline), first bullet

The following procedures/assessments will be performed:

- Obtain written informed consent for DV0002 and PS0014 (may be obtained prior to Visit 1).

Has been changed to:

The following procedures/assessments will be performed:

- Obtain written informed consent ~~for DV0002 and PS0014~~ (may be obtained prior to Visit 1).

Change #27

New Section 8.2 Treatment Period for 2mL Device Presentation Cohort and new subsections 8.2.1 through 8.2.6 added as follows:

8.2 Treatment Period for 2mL Device Cohort

For the 2mL device cohort, DV0002 Visit 1 (Baseline) will occur at PS0014 Week 24, Week 28, or Week 32 for subjects receiving bimekizumab Q4W or Week 24 or Week 32 for subjects receiving bimekizumab Q8W.

8.2.1 Visit 1 (Baseline)

For DV0002 Visit 1 (Baseline) study assessments, refer to Table 5-4 and perform the assessments for the week that the subject starts the DV0002 substudy (PS0014 Week 24, Week 28, or Week 32 for bimekizumab Q4W or Week 24 or Week 32 for bimekizumab Q8W). In addition to the PS0014 study assessments, the following assessments will be performed at the Baseline visit of DV0002 (Table 5-5):

- **Informed consent for DV0002.**
- **Random assignment to device (DV0002-specific).**
- **IRT contact.**
- **Blood sample for bimekizumab plasma concentrations.**
- **Subject training for VAS and SIAQ Questionnaire (version 2.0 for bimekizumab-SS-2mL and version 2.1 for bimekizumab-AI-2mL) (DV0002-specific).**
- **Complete the pre-injection SIAQ Questionnaire (DV0002-specific).**
- **Subject training for self-injection (DV0002-specific).**
- **Subject self-injection of bimekizumab using the assigned device (DV0002-specific).**
- **Study personnel evaluation of self-injection (DV0002-specific).**

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- **Complete the VAS for injection site pain (DV0002-specific).**
- **Complete the post-injection SIAQ Questionnaire (version 2.0 for bimekizumab-SS-2mL and version 2.1 for bimekizumab-AI-2mL) (DV0002-specific).**
- **Study personnel evaluation of device for structural/mechanical integrity (DV0002-specific).**
- **Drug and device accountability (DV0002-specific).**

8.2.2 Visit 2 (Baseline + 4 weeks)

For PS0014 study assessments, refer to Table 5-4. In addition, perform the following DV0002 substudy assessments:

- **IRT contact.**
- **Blood sample for bimekizumab plasma concentrations (DV0002-specific)—only done for subjects who receive bimekizumab Q4W.**
- **Bimekizumab administration by study personnel using the PFS—only done for subjects who receive bimekizumab Q4W.**
- **Drug and device accountability (DV0002-specific)—only done for subjects who receive bimekizumab Q4W.**

8.2.3 Visit 3 (Baseline + 8 weeks)

For PS0014 study assessments, refer to Table 5-4. In addition, perform the following DV0002 substudy assessments:

- **IRT contact.**
- **Blood sample for bimekizumab plasma concentrations (DV0002-specific).**
- **Subject self-injection of bimekizumab using the assigned device (DV0002-specific).**
- **Study personnel evaluation of self-injection (DV0002-specific).**
- **Complete the VAS for injection site pain (DV0002-specific).**
- **Complete the post-injection SIAQ Questionnaire (version 2.0 for bimekizumab-SS-2mL and version 2.1 for bimekizumab-AI-2mL) (DV0002-specific).**
- **Study personnel evaluation of device for structural/mechanical integrity (DV0002-specific).**
- **Drug and device accountability (DV0002-specific).**

8.2.4 Visit 3a (Baseline + 9 weeks; safety follow-up telephone call)

Visit 3a (Week 9) will occur in the DV0002 substudy but not in the PS0014 study. The following procedures/assessments will be performed:

- **Concomitant medications.**
- **Adverse events.**

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8.2.5 Visit 4 (Baseline + 12 weeks)

For PS0014 study assessments, refer to Table 5-4. In addition, perform the following DV0002 substudy assessments:

- **IRT contact.**
- **Blood sample for bimekizumab plasma concentrations (DV0002-specific)—only done for subjects who receive bimekizumab Q4W.**
- **Bimekizumab administration by study personnel using the PFS—only done for subjects who receive bimekizumab Q4W.**
- **Drug and device accountability (DV0002-specific).**

8.2.6 Visit 5 (Baseline + 16 weeks)

For PS0014 study assessments, refer to Table 5-4. In addition, perform the following DV0002 substudy assessments:

- **IRT contact.**
- **Blood sample for bimekizumab plasma concentrations (DV0002-specific)—only done for subjects who receive bimekizumab Q8W.**
- **Bimekizumab administration by study personnel using the PFS. (If this visit coincides with Week 48 of PS0014, subjects will have the option to self-inject; refer to the PS0014 protocol.)**
- **Drug and device accountability (DV0002-specific).**

Change #28

Section 9.1 Assessment of self-injection experience by SIAQ, paragraph 2 and 3

The SIAQ was developed by UCB to assess the perceived advantages and the potential limitations of self-injection of an sc medication (Keininger and Coteur, 2011). The pre-injection SIAQ is composed of 7 items grouped into 3 domains (feelings about injection, self-confidence, and satisfaction with the current mode of administration). The post-injection SIAQ is composed of 21 items grouped into 6 domains (feelings about injection, self-image, self-confidence, injection site reactions, ease of use, and satisfaction with self-injection). The pre-injection SIAQ will be completed at Visit 1, and the post-injection SIAQ will be completed within 30 minutes after each self-injection (ie, at Visit 1 and Visit 3).

Version 2.0 and version 2.1 of the SIAQ are identical, except for Question 11. In version 2.0 of the SIAQ, Question 11 discusses the use of a plunger, while in version 2.1 of the SIAQ, Question 11 discusses depression of the device. Version 2.0 will therefore be used to assess bimekizumab-SS-1mL, while version 2.1 will be used to assess bimekizumab-AI-1mL.

Has been changed to:

The SIAQ was developed by UCB to assess the perceived advantages and the potential limitations of self-injection of an sc medication (Keininger and Coteur, 2011). The pre-injection SIAQ is composed of 7 items grouped into 3 domains (feelings about injection, self-confidence, and satisfaction with the current mode of administration). The post-injection SIAQ is composed

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of 21 items grouped into 6 domains (feelings about injection, self-image, self-confidence, injection site reactions, ease of use, and satisfaction with self-injection). The pre-injection SIAQ will be completed at Visit 1, and the post-injection SIAQ will be completed within 30 minutes after ~~each~~ self-injection (ie, at Visit 1 and Visit 3). **For the 1mL device cohort, the SIAQ will be completed within 30 minutes of completing the second injection. For the 2mL device cohort, the SIAQ will be completed within 30 minutes of completing the single injection.**

Version 2.0 and version 2.1 of the SIAQ are identical, except for Question 11. In version 2.0 of the SIAQ, Question 11 discusses the use of a plunger, while in version 2.1 of the SIAQ, Question 11 discusses depression of the device. Version 2.0 will therefore be used to assess bimekizumab-SS-1mL **and bimekizumab-SS-2mL**, while version 2.1 will be used to assess bimekizumab-AI-1mL **and bimekizumab-AI-2mL**.

Change #29

Section 9.2 Assessment of injection site pain

A VAS will be used to assess overall injection pain due to self-injection at Baseline and at Week 8. Subjects will be required to indicate their injection pain by placing a mark on a 100mm line from 0 (no pain) to 100 (worst possible pain). In the DV0002 substudy, the 320mg bimekizumab dose will be administered as two 160mg sc injections with either 2 bimekizumab-SS-1mL or 2 bimekizumab-AI-1mL devices. To evaluate injection pain for both self-injections, the VAS will be assessed immediately (within 15 minutes) after completion of the second self-injection. The subject will complete the VAS prior to completion of the post-injection SIAQ (refer to Section 9.1 for details).

Has been changed to:

A VAS will be used to assess overall injection pain due to self-injection at **DV0002** Baseline and at ~~Week~~ 8 **weeks after training**. Subjects will be required to indicate their injection pain by placing a mark on a 100mm line from 0 (no pain) to 100 (worst possible pain).

1mL Device Cohort

In the 1mL device cohort of the DV0002 substudy, the 320mg bimekizumab dose will be administered as two 160mg sc injections with either 2 bimekizumab-SS-1mL or 2 bimekizumab-AI-1mL devices. To evaluate injection pain for both self-injections, the VAS will be assessed immediately (within 15 minutes) after completion of the second self-injection. The subject will complete the VAS prior to completion of the post injection SIAQ (refer to Section 9.1 for details).

2mL Device Cohort

In the 2mL device cohort, the 320mg bimekizumab dose will be administered as 1 sc injection with either the bimekizumab-SS-2mL or bimekizumab-AI-2mL device. To evaluate injection pain for the self-injection, the VAS will be assessed immediately (within 15 minutes) after completion of the self-injection. The subject will complete the VAS prior to completion of the post-injection SIAQ (refer to Section 9.1 for details).

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Change #30

Section 9.3 Evaluation of post-use structural and mechanical integrity of self-injection device presentations

The visual inspection of the used bimekizumab-SS-1mL and bimekizumab-AI-1mL devices will check for structural/mechanical integrity and damage (ie, clear evidence of damage/compromised structural integrity and not any superficial, cosmetic imperfections). All evaluations will be performed by appropriately trained site staff. Any device with structural/mechanical integrity issues will be returned to UCB for further evaluation. Superficial, cosmetic imperfections which have no impact on structural or mechanical integrity are to be ignored.

Has been changed to:

The visual inspection of the used ~~bimekizumab-SS-1mL and bimekizumab-AI-1mL~~ devices will check for structural/mechanical integrity and damage (ie, clear evidence of damage/compromised structural integrity and not any superficial, cosmetic imperfections). All evaluations will be performed by appropriately trained site staff. Any device with structural/mechanical integrity issues will be returned to UCB for further evaluation. Superficial, cosmetic imperfections which have no impact on structural or mechanical integrity are to be ignored.

Used devices that functioned as intended and which had no post-use structural or mechanical integrity issues (as determined by the post-use site evaluation) will also be returned to UCB for further evaluation.

Change #31

Section 10 Assessment of Pharmacokinetic Variables

Blood samples for measurement of trough bimekizumab PK (Section 4.1.3) will be collected at the time points specified in the schedule of study assessments (Table 5-2).

At dosing visits, blood samples will be drawn prior to dosing (at the same time of the sampling for clinical laboratory tests). The time and date of collection will be recorded in the eCRF.

Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the laboratory manual for this study. Detailed information on sample analysis will be provided in a bioanalytical report.

Has been changed to:

1mL Device Cohort

Blood samples for measurement of trough bimekizumab PK (Section 4.1.3**.2**) will be collected at the time points specified in the schedule of study assessments (Table 5-~~2~~**3**).

At dosing visits, blood samples will be drawn prior to dosing (at the same time of the sampling for clinical laboratory tests). The time and date of collection will be recorded in the eCRF.

Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the laboratory manual for this study. Detailed information on sample analysis will be provided in a bioanalytical report.

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2mL Device Cohort

For subjects who participate in the 2mL device cohort, blood samples for measurement of trough bimekizumab PK levels (Section 4.1.3.2) will be collected at the timepoints specified in Table 10-1.

Table 10-1: DV0002 substudy 2mL device cohort PK sample collection time points

Dose Regimen	PS0014 Week that subject starts DV0002	DV0002 Visits				
		Visit 1 (Baseline)/ Week 0	Visit 2/ Week 4	Visit 3/ Week 8	Visit 4/ Week 12	Visit 5/ Week 16
320mg Q4W	Week 24	X[a]	X	X	X	X[a]
	Week 28	X	X	X	X[a]	NA
	Week 32	X	X	X	X	X[a]
320mg Q8W	Week 24	X[a]	NA	X	NA	X[a]
	Week 32	X	NA	X[a]	NA	X[a]

NA=not applicable; PK=pharmacokinetics; Q4W=every 4 weeks; Q8W=every 8 weeks
Note: For the 2mL device cohort, the DV0002 Baseline visit will be PS0014 Week 24, Week 28, or Week 32 for subjects receiving bimekizumab 320mg Q4W or PS0014 Week 24 or Week 32 for subjects receiving bimekizumab 320mg Q8W.
[a] PK sample taken per the PS0014 schedule.

At dosing visits, blood samples will be drawn prior to dosing (at the same time of the sampling for clinical laboratory tests). The time and date of collection will be recorded in the eCRF.

Instructions pertaining to sample collection, processing, storage, labeling, and shipping are provided in the laboratory manual for this study. Detailed information on sample analysis will be provided in a bioanalytical report.

Change #32

Section 11.1 Adverse events (investigational device)

All AEs (including serious adverse events [SAEs]) will be reported in a common database for PS0014 and DV0002, but only ADEs, 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; please refer to the PS0014 protocol for information on reporting and recording AEs (including SAEs).

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Has been changed to:

All AEs (including serious adverse events [SAEs]) will be reported in a common database for PS0014 and DV0002, but only ADEs, 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; please refer to the PS0014 protocol for information on reporting and recording AEs (including SAEs).

Change #33

Section 13.3.1 Case Report form completion, paragraph 1

This study is performed using remote data capture. The Investigator is responsible for prompt reporting of accurate, complete, and legible data in the eCRFs and in all required reports.

Has been changed to:

This study is performed using remote data capture**; the same data capture is used for PS0014 and DV0002**. The Investigator is responsible for prompt reporting of accurate, complete, and legible data in the eCRFs and in all required reports.

Change #34

Section 14 Statistics

A description of statistical methods follows and will be described in more detail in the Statistical Analysis Plan (SAP).

Has been changed to:

A description of statistical methods follows and will be described in more detail in the Statistical Analysis Plan (SAP).

Once subjects in the 1mL device cohort complete DV0002, a final analysis for that cohort will be performed, and a clinical study report will be prepared. A separate final analysis will be performed for the 2mL device cohort.

Change #35

Section 14.1 Definition of analysis sets

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.

Two different Full Analysis Sets (FASs) will be generated (1 for each device type): the bimekizumab-SS-1mL Full Analysis Set (FAS-s) and the bimekizumab-AI-1mL Full Analysis Set (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.

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Two different Pharmacokinetic Sets (PKS) will be generated (1 for each device type): the bimekizumab-SS-1mL PKS (PKS-s) and the bimekizumab-AI-1mL PKS (PKS-a). Each PKS 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. Pharmacokinetic variables will be analyzed using the PKS-s and PKS-a.

Has been changed to:

1mL Device Cohort

For the 1mL device cohort, 2 ~~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.

Two different Full Analysis Sets (FASs) will be generated (1 for each device type): the bimekizumab-SS-1mL Full Analysis Set (FAS-s) and the bimekizumab-AI-1mL Full Analysis Set (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.

~~Two~~**For the PK analyses, 2** different Pharmacokinetic **Per Protocol** Sets (~~PKS~~**PK-PPS**) will be generated (1 for each device type): the bimekizumab-SS-1mL ~~PKS (PKS~~**PK-PPS** (**PK-PPS**-s) and the bimekizumab-AI-1mL ~~PKS (PKS~~ **PK-PPS (PK-PPS**-a). Each ~~PKS~~**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 ~~PKS~~ **PK-PPS**-s and ~~PKS~~**PK-PPS**-a.

All PK assessments after baseline assessments from feeder study will be considered for the requirement of at least 1 evaluable PK assessment.

2mL Device Cohort

For the 2mL device cohort, the same analysis sets will be generated.

Change #36

Section 14.3 Planned analyses of outcome variables

All statistical analyses will be descriptive in nature. No inferential statistical analyses are planned.

Has been changed to:

All statistical analyses will be descriptive in nature. No inferential statistical analyses are planned.

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

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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 #37

Section 14.3.1 Analysis of the primary outcome variable, paragraph 1

The primary outcome variable is the percentage of all subjects able to self-administer safe and effective injections using the given device presentation at Week 8. Safe and effective self-injection will be evaluated by the study personnel as defined in in Section 4.1.1.

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 presentation at **DV0002** Week 8 **(8 weeks after training)**. Safe and effective self-injection will be evaluated by the study personnel as defined in in Section 4.1.1.

Change #38

Section 14.4 Planned pharmacokinetic analyses

The statistical analyses of the PK data will be descriptive in nature and will be summarized using the relevant device-specific population (PKS-s or PKS-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. Three BMI categories will be defined based on tertiles 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.

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 (~~PKS~~**PK-PPS**-s or ~~PKS~~**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. Three BMI categories will be defined based on tertiles derived from subjects' Baseline BMI values **within the device-specific population (PK-PPS-s or PK-PPS-a)**.

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 Week 8 for the study personnel administration and at **DV0002** 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 **DV0002**

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Baseline for the study personnel administration and at **8 weeks after training (DV0002 Week 8)** and **DV0002** 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.

Change #39

Section 14.9 Planned interim analysis and data monitoring

The final DV0002 substudy analysis and clinical study report will be prepared once all data have been collected. No Data Monitoring Committee will be established for this study.

Has been changed to:

~~The final DV0002 substudy~~ **No interim** analysis ~~and clinical~~ **is planned for the DV0002** study ~~report will be prepared once all data have been collected~~. 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 ADEs and ongoing concomitant medication.

Change #40

Section 14.10 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 in 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 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.

Has been changed to:

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

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1mL Device Cohort

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 in 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.

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. 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.

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19 DECLARATION AND SIGNATURE OF INVESTIGATOR

I confirm that I have carefully read and understood this protocol and agree to conduct this clinical study as outlined in this protocol, according to current Good Clinical Practice and local laws and requirements.

I will ensure that all subinvestigators and other staff members read and understand all aspects of this protocol.

I have received and read all study-related information provided to me.

The objectives and content of this protocol as well as the results deriving from it will be treated confidentially and will not be made available to third parties without prior authorization by UCB.

All rights of publication of the results reside with UCB, unless other agreements were made in a separate contract.

Investigator:

Printed name	Date/Signature

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20 SPONSOR DECLARATION

I confirm that I have carefully read and understand this protocol and agree to conduct this clinical study as outlined in this protocol and according to current Good Clinical Practice.

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Approval Signatures

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Document Approvals	
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