PROTOCOL DV0004 AMENDMENT 1

(NORTH AMERICA AND EU SUBSTUDY TO PA0012)

A MULTICENTER, RANDOMIZED, OPEN-LABEL STUDY TO EVALUATE THE SAFE AND EFFECTIVE USE OF THE PREFILLED SAFETY SYRINGE OR AUTO-INJECTOR FOR THE SUBCUTANEOUS SELF-INJECTION OF BIMEKIZUMAB SOLUTION BY SUBJECTS WITH ACTIVE PSORIATIC ARTHRITIS

PHASE 3

IND Number: 128708

EudraCT number: 2018-004725-86

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Protocol/Amendment number	Date	Type of amendment
Final protocol	05 Feb 2019	Not applicable
Protocol Amendment 1	14 May 2020	Nonsubstantial

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LIST OF ABBREVIATIONS

ADE	adverse device effect
AE	adverse event
bimekizumab-AI-1mL	1mL bimekizumab auto-injector
bimekizumab-SS-1mL	1mL bimekizumab safety syringe
BMI	body mass index
CDMS	clinical data management system
CI	confidence interval
CRO	contract research organization
ECG	electrocardiogram
eCRF	electronic Case Report form
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
IEC	Independent Ethics Committee
IFU	instructions for use
IL	interleukin
IMP	investigational medicinal product
IRB	Institutional Review Board
IRT	interactive response technology
PFS	prefilled syringe
PK	pharmacokinetic(s)
PKS	Pharmacokinetic Set
PKS-a	Pharmacokinetic Set for the bimekizumab-AI-1mL
PKS-s	Pharmacokinetic Set for the bimekizumab-SS-1mL
PS	Patient Safety
PsA	psoriatic arthritis
Q4W	every 4 weeks
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
SS-s	Safety Set for the bimekizumab-SS-1mL
USADE	unanticipated serious adverse device effect
VAS	visual analog scale

1 SUMMARY

DV0004 is a Phase 3, multicenter, open-label, randomized, noncomparator, North America and Europe substudy to PA0012 in adult subjects with active psoriatic arthritis (PsA) to evaluate the safe and effective use of 2 single-use disposable self-injecting device presentations for the subcutaneous (sc) administration of bimekizumab solution (the investigational medicinal product [IMP]). To provide patients with PsA with options for the self-administration of bimekizumab, DV0004 will evaluate 2 investigational self-injecting device presentations, which are drug product (IMP) associated with a functional secondary packaging: the 1mL bimekizumab safety syringe (bimekizumab-SS-1mL) and the 1mL bimekizumab auto-injector (bimekizumab-AI-1mL).

DV0004 is a substudy of PA0012, which is a multicenter, open-label, long-term safety study for subjects with PsA who complete 1 of the Phase 3 feeder studies (PA0010 or PA0011). The PA0012 study will evaluate the long-term safety, tolerability, and efficacy of bimekizumab in subjects with PsA, and study personnel qualified in sc injection technique will administer bimekizumab to subjects (except for specified study visits at which subjects may self-administer) in a 1mL True North prefilled syringe (referred to throughout this protocol as the 1mL PFS). Subjects will begin the DV0004 substudy and the PA0012 study at the same time. The DV0004 substudy will include all PA0012 study assessments from Baseline to Week 4 (inclusive). However, subjects in the DV0004 substudy will self-administer bimekizumab at Baseline and at Week 4.

During the 4-week Treatment Period of DV0004, subjects will receive bimekizumab 160mg every 4 weeks (Q4W). This dose regimen will remain stable for the entire 4-week Treatment Period of DV0004 (consistent with PA0012). In the DV0004 substudy, subjects will be randomly assigned to 1 of the 2 self-injecting device presentations and will self-administer bimekizumab at Baseline and at Week 4. A safety follow-up (SFU) telephone call will occur 1 week after the last self-administration in DV0004 (Week 5). After Week 5 in the DV0004 substudy, subjects will continue in PA0012 (the next visit after DV0004 completion will be the Week 8 Visit in PA0012). At Week 8 in PA0012, study personnel qualified in sc injection technique will administer bimekizumab to subjects in a 1mL PFS, or the subject/caregiver/appropriate designee will perform administration under the supervision of the site staff after training.

To compensate for subjects who have different study treatments between the feeder studies and DV0004, DV0004 is planned to enroll approximately 200 subjects (100 subjects per device presentation arm) to ensure that approximately 50 subjects per device presentation arm are evaluable for steady state trough pharmacokinetic (PK) level analyses. Within each device presentation 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 DV0004 substudy is to evaluate for each self-injecting device presentation the ability of subjects with PsA to safely and effectively self-inject bimekizumab 4 weeks after training in 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 at Week 4.

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 presentation for self-injection (ie, no serious adverse device effects [SADEs] and/or ADEs leading to withdrawal from the DV0004 substudy)

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 presentation, 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 4.1.3.4, respectively.

2 INTRODUCTION

Psoriatic arthritis 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 PsA, psoriasis, and axial spondyloarthritis.

It is important for patients who may use bimekizumab for the treatment of active PsA 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 of skin penetration by needle, control 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 two different options to self-inject bimekizumab.

The DV0004 study is a substudy of the PA0012 study. PA0012 will evaluate the long-term safety, tolerability, and efficacy of bimekizumab in subjects with PsA; study personnel will administer bimekizumab in a 1mL PFS (except at specified study visits at which subjects may self-administer). The DV0004 substudy will evaluate 2 self-injecting device presentations: the 1mL bimekizumab-SS-1mL and the 1mL bimekizumab-AI-1mL. Subjects will begin the DV0004 substudy and the PA0012 study at the same time. The DV0004 substudy will include all PA0012 study assessments from Baseline to Week 4 (inclusive). However, subjects in the DV0004 substudy will self-administer bimekizumab at Baseline and at Week 4.

In the DV0004 substudy, the self-injecting device presentations are drug product (IMP) associated with a functional secondary packaging (either the bimekizumab-SS-1mL or bimekizumab-AI-1mL). The bimekizumab-SS-1mL and the bimekizumab-AI-1mL are each single integral units which are intended exclusively for use in the given combination and are not reusable. Therefore, compliance to the EU Medical Device Regulation (except for Annex 1) and European Conformity marking (CE marking) is not foreseen. 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 PsA can safely and effectively self-inject bimekizumab using the bimekizumab-SS-1mL or the bimekizumab-AI-1mL.

3 STUDY OBJECTIVES

3.1 Primary objective

The primary objective of the study is to evaluate for each self-injecting device presentation the ability of subjects with PsA to safely and effectively self-inject bimekizumab 4 weeks after training in self-injection technique using the bimekizumab-SS-1mL or the bimekizumab-AI-1mL.

3.2 Secondary objective

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

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) for injection site pain and the Self-injection Assessment Questionnaire (SIAQ)
- Trough PK (trough bimekizumab) levels associated with self-injection using the test self-injecting device presentations, injection by study personnel using the 1mL PFS, injection site (abdomen or thigh), and BMI category (by tertile)
- Immunogenicity of bimekizumab associated with self-injection using the self-injecting device presentations and injection by study personnel using the 1mL PFS
- The structural and mechanical integrity of the bimekizumab-SS-1mL and the bimekizumab-AI-1mL after completion of self-injection
- The functional integrity of the bimekizumab-SS-1mL and the bimekizumab-AI-1mL after completion of self-injection
- The overall safety and tolerability of self-injections using the self-injecting device presentations

4 STUDY VARIABLES

4.1 Outcome variables

4.1.1 Primary outcome variable

The primary outcome variable is the ability to self-administer safe and effective injections using the bimekizumab-SS-1mL or the bimekizumab-AI-1mL at Week 4. 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 presentations for self-injection (ie, no SADEs and/or ADEs leading to withdrawal from the DV0004 substudy).

4.1.2 Secondary outcome variable

The secondary outcome variable is the ability 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 using the same criteria as 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 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).
- Injection site pain (using a VAS; 100mm) by visit after self-injection using the assigned self-injecting device presentations at Baseline and Week 4
- Responses to post-injection SIAQ (versions 2.0 and 2.1) by visit following self-injection using the assigned self-injecting device presentations at Baseline and Week 4
- The structural and mechanical integrity of the bimekizumab-SS-1mL and the bimekizumab-AI-1mL after completion of self-injection using the assigned self-injecting device presentations
- The functional integrity of the bimekizumab-SS-1mL and the bimekizumab-AI-1mL after completion of self-injection using the assigned self-injecting device presentations

4.1.3.2 Pharmacokinetic variable

The PK variable is trough PK (bimekizumab) levels associated with self-injection using the test self-injecting device presentations, 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, and Week 8 (in PA0012).

4.1.3.3 Immunological variable

The immunological variable is the anti-bimekizumab antibody, which will be collected as described in the PA0012 protocol.

4.1.3.4 Safety variable

The other safety variable is the occurrence of ADEs. Additional safety and tolerability variables will be collected as described in the PA0012 protocol.

5 STUDY DESIGN

5.1 Study description

DV0004 is a Phase 3, multicenter, open-label, randomized, noncomparator, North America and Europe substudy to PA0012. PA0012 will evaluate the long-term safety, tolerability, and efficacy of bimekizumab in adult subjects with PsA. In the DV0004 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 adult subjects with PsA will be evaluated.

Subjects from sites in the PA0012 feeder studies, PA0010 and PA0011, will be eligible for the DV0004 substudy. The DV0004 substudy will maintain all study assessments of the main PA0012 study from Baseline to Week 4 (inclusive). However, only subjects in the DV0004

substudy will self-administer bimekizumab using the bimekizumab-SS-1mL or the bimekizumab-AI-1mL at Baseline and Week 4. At DV0004 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 DV0004 substudy will perform self-injections at the DV0004 Baseline (corresponding to the Entry Visit of PA0012) with a subsequent self-injection at the DV0004 Week 4 Visit (corresponding to Week 4 of PA0012).

During the 4-week Treatment Period of DV0004, subjects will receive bimekizumab 160mg Q4W. This dose regimen will remain stable for the entire 4-week Treatment Period of DV0004 (consistent with PA0012). The DV0004 substudy will evaluate 2 self-injecting device presentations: the bimekizumab-SS-1mL and the bimekizumab-AI-1mL. Baseline for DV0004 and the Entry Visit for PA0012 will occur at the same time, and the same interactive response technology (IRT) will be used for both studies.

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). Subjects will perform self-injection with the assigned device presentation at Baseline (corresponding to the Entry Visit of PA0012) and at Week 4 (corresponding to Week 4 of PA0012).

At Baseline, Week 4, and Week 8 (of PA0012), pre-injection blood samples for PK trough analysis will be collected. At Baseline and Week 4, subjects will self-inject 160mg bimekizumab using the assigned device presentation. Bimekizumab PK trough levels associated with injection by study personnel using the 1mL PFS (in PA0010 or PA0011) will be analyzed from the pre-injection PK sample collected at Baseline. Bimekizumab PK trough levels associated with subject self-injection using the assigned self-injecting device presentation will be analyzed from the pre-injection PK samples collected at Week 4 and Week 8 (of PA0012).

In addition to self-injections, DV0004 substudy-specific assessments (eg, study personnel evaluation of safe and effective self-injection, VAS for injection site pain, SIAQ responses, and PK analyses; see Section 5.2) will be performed from Baseline through Week 4 (inclusive). An SFU telephone call will occur 1 week after the last self-administration in DV0004.

After Week 5 of the DV0004 substudy, subjects will continue in PA0012 (the next visit after DV0004 completion will be the Week 8 Visit in PA0012). At Week 8 in PA0012, study personnel qualified in sc injection technique will administer bimekizumab to subjects in a 1mL PFS, or the subject/caregiver/appropriate designee will perform administration under the supervision of the site staff after training. Studies DV0004 and PA0012 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 DV0004 but continue their PA0012 study participation will be required to perform an SFU telephone call 1 week after their final DV0004 dosing visit (see Section 6.3). Subjects who are withdrawn from bimekizumab treatment (PA0012 study) during the course of DV0004 will also be required to follow the PA0012 withdrawal procedures.

5.1.1 Study duration per subject

The maximum DV0004 substudy duration will be 5 weeks for each subject. Subjects will then continue to receive treatment in PA0012 for the duration of the PA0012 study.

The end of the DV0004 substudy is defined as the date on which the last subject completes his/her Week 5 Visit or withdraws from the study.

5.1.2 Planned number of subjects and sites

It is planned to enroll approximately 200 subjects; each device presentation arm will consist of approximately 100 subjects. It is anticipated that this study will involve up to 150 sites in North America and Europe.

5.1.3 Anticipated regions and countries

This substudy will be conducted in North America and Europe.

5.2 Schedule of study assessments

The schedule of assessments for DV0004 is presented in Table 5–1 and includes assessments performed specifically in the DV0004 substudy. The schedule of assessment for PA0012 Entry Visit through Week 8 is presented in Table 5–2 and includes assessments performed as part of the PA0012 study.

Table 5–1: Schedule of study assessments for DV0004

Visit [a] / Week / Procedures	Visit 1	Visit 2	Visit 2a Telephone Call (Device SFU)
	Baseline/ Feeder Study Final Visit	Week 4	Week 5
Informed consent for DV0004 assessments	X		
Inclusion/exclusion	X		
Concomitant medication	X	X	X
Adverse events [b]	X	X	X
Random assignment to device presentation	X		
IRT contact	X	X	X
Subject training for VAS and SIAQ Questionnaire	X		
Pre-injection SIAQ Questionnaire [c]	X		
Subject training for self-injection	X		
Subject self-injection of bimekizumab using the assigned device presentation	X	X	
Study personnel evaluation of self-injection	X	X	
Study personnel evaluation of post-use device presentation for visual signs of structural or mechanical integrity (such as cracks or loose parts) [d]	X	X	
VAS for injection site pain	X	X	
Post-injection SIAQ Questionnaire [c]	X	X	
Drug and device presentation accountability	X	X	

IRT=interactive response technology; SFU=safety follow-up; SIAQ=Self-injection Assessment Questionnaire; VAS=visual analog scale

[a] Visit windows are ±7 days from the scheduled visit day (relative to the first dose) at all visits except Visit 2a (SFU telephone call). The SFU telephone call window is 7 days from the last dose in the DV0004 substudy, ±3 days.

Table 5–1: Schedule of study assessments for DV0004

Visit [a] / Week / Procedures	Visit 1	Visit 2	Visit 2a Telephone Call (Device SFU)
	Baseline/ Feeder Study Final Visit	Week 4	Week 5

[b] Adverse events not related to the device presentations will be reported in PA0012 and adverse device effects and device deficiencies will be reported in DV0004. A single safety database will be used for both studies.

[c] 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).

[d] Device presentations with visual signs of compromised structural or mechanical integrity should be returned to UCB after use. Used device presentations that functioned as intended (ie, complete dose delivered, no visual signs of compromised structural or mechanical integrity) should be stored at room temperature in a secured area and may only be destroyed following UCB's instruction.

Table 5–2: Schedule of study assessments for corresponding visits in PA0012

Visit [a] / Week / Procedures	Visit 1	Visit 2	Visit 3
	Entry Visit/ Feeder Study Final Visit	Week 4	Week 8
Informed consent PA0012 assessments	X		
Inclusion/exclusion	X		
Concomitant medication	X	X	X
PHQ-9	X		
eC-SSRS	X	X	X
Body weight	X		
Vital signs (pulse, temperature, BP) [b]	X	X	X
ECG by central reader	X		
Hematology/biochemistry/urine pregnancy [c, d]	X	X	X
Blood Sample for hs-CRP [d]	X	X	X
Blood sample for bimekizumab plasma concentrations [c, d]	X	X	X
Blood sample for anti-bimekizumab antibodies [d]	X	X	X
IGRA TB test	X [e]		
TB questionnaire	X		
Physical examination [f]	X		
BSA affected by PSO (BSA palm method)	X		
PASI [g]	X		
IGA [g]	X		
TJC (68) and SJC (66)	X		

Table 5–2: Schedule of study assessments for corresponding visits in PA0012

Visit [a] / Week / Procedures	Visit 1	Visit 2	Visit 3
	Entry Visit/ Feeder Study Final Visit	Week 4	Week 8
HAQ-DI	X		
PtAAP	X		
PhGA-PsA	X		
PhGA-Arthritis	X		
PGA-PsA	X		
PGA-Arthritis	X		
BASDAI	X		
mNAPSI	X		
LEI/SPARCC	X		
LDI	X		
PSAID-12	X		
FACIT-F	X		
SF-36	X		
EQ-5D-3L	X		
WPAI-SHP	X		
Adverse events [h]	X	X	X
IRT contact	X	X	X
Bimekizumab administration by study personnel using the PFS			X

Table 5–2: Schedule of study assessments for corresponding visits in PA0012

Visit [a] / Week / Procedures	Visit 1	Visit 2	Visit 3
	Entry Visit/ Feeder Study Final Visit	Week 4	Week 8

BASDAI=Bath Ankylosing Spondylitis Disease Activity Index; BP=blood pressure; BSA=body surface area; ECG=electrocardiogram; eC-SSRS=electronic Columbia Suicide Severity Rating Scale; EQ-5D-3L=Euro-Quality of Life 5-Dimensions 3-level; FACIT-F=Functional Assessment of Chronic Illness Therapy—Fatigue; HAQ-DI=Health Assessment Questionnaire-Disability Index; hs-CRP=high sensitivity C-reactive protein; IGA=Investigator's Global Assessment; IGRA=interferon-gamma release assay; IRT=interactive response technology; LDI=Leeds Dactylitis Index; LEI=Leeds Enthesitis Index; mNAPSI=modified Nail Psoriasis Severity Index; PASI=Psoriasis Area Severity Index; PGA-Arthritis=Patient's Global Assessment of Arthritis; PGA-PsA=Patient's Global Assessment of Psoriatic Arthritis; PhGA-Arthritis=Physician's Global Assessment of Arthritis; PhGA-PsA=Physician's Global Assessment of Psoriatic Arthritis; PHQ-9=Patient Health Questionnaire 9; PsAID=Psoriatic Arthritis Impact of Disease; PSO=psoriasis; PtAAP=Patient's Assessment of Arthritis Pain; Q4W=every 4 weeks; SF-36=Short Form 36-item Health Survey; SFU=safety follow-up; SIAQ=Self-injection Assessment Questionnaire; SJC=swollen joint count; SPARCC=Spondyloarthritis Research Consortium of Canada; TB=tuberculosis; TJC=tender joint count; VAS=visual analog scale; WPAI-SHP=Work Productivity and Activity Impairment Questionnaire-specific health problem

[a] Visit windows are ±7 days from the scheduled visit day (relative to the first dose) at all visits with a minimum of 21 days and a maximum of 35 days in between bimekizumab doses.

[b] Adverse events not related to the device presentations will be reported in PA0012 and adverse device effects and device deficiencies will be reported in DV0004. A single safety database will be used for both studies.

[c] If there has been a delay in menses, perform a urine pregnancy test.

[d] All blood samples are to be taken prior to bimekizumab dosing.

[e] This assessment only needs to be performed at study entry if an IGRA negative result is not available from less than 6 weeks prior to the first dose of open label bimekizumab.

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

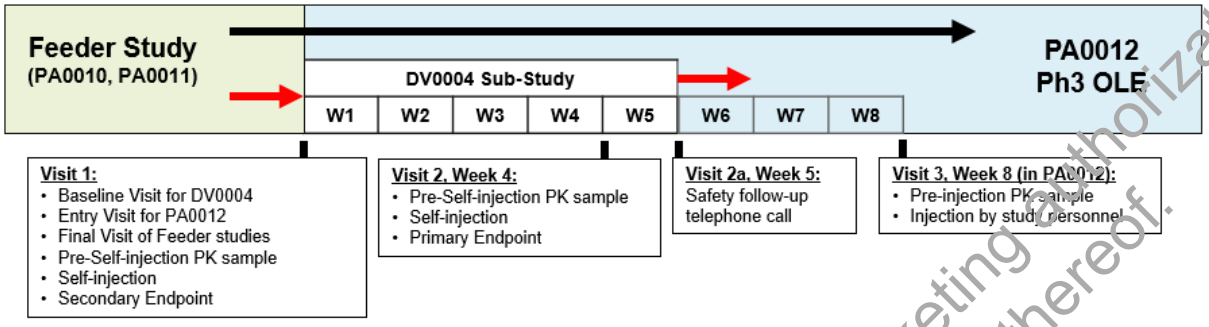
[g] If the BSA affected by PSO was ≥3% at Baseline from PA0010 or PA0011, determine the PASI and IGA.

[h] Adverse events not related to the device presentations will be reported in PA0012 and adverse device effects and device deficiencies will be reported in DV0004. A single safety database will be used for both studies.

5.3 Schematic diagram

The study schematic diagram for DV0004 is presented in Figure 5–1.

Figure 5–1: Schematic diagram



OLE=open-label extension; Ph3=Phase 3; PK=pharmacokinetic; W=Week
Note: The DV0004 substudy ends after the Week 5 SFU phone call. The Week 8 pre-injection PK sample is collected in PA0012.

5.4 Rationale for study design and selection of dose

DV0004 is a Phase 3, multicenter, open-label, randomized, noncomparator, North America and Europe substudy to PA0012 for subjects with PsA who will self-inject bimekizumab. PA0012 is a multicenter, open-label, long-term study to evaluate the safety, tolerability, and efficacy of bimekizumab in subjects with PsA who complete 1 of the Phase 3 feeder studies (PA0010, PA0011).

It is expected that most individuals who will use commercial bimekizumab for the treatment of PsA will self-inject bimekizumab and also that these individuals will prefer to have options for the self-administration of their medication. DV0004 will therefore evaluate the safe and effective use of 2 different self-injecting device presentations: bimekizumab-SS-1mL and bimekizumab-AI-1mL. In addition, DV0004 will assess trough PK levels associated with self-injection using the test self-injecting device presentation, injection by study personnel using the 1mL PFS, injection site (abdomen or thigh), by anti-bimekizumab antibody status, and BMI category (by tertile).

6 SELECTION AND WITHDRAWAL OF SUBJECTS

6.1 Inclusion criteria

To be eligible for DV0004, subjects must meet all of the following criteria:

1. An Institutional Review Board (IRB)/Independent Ethics Committee (IEC) approved written Informed Consent form (ICF) for DV0004 is signed and dated by the subject.
2. Subject fulfills all inclusion criteria for the PA0012 study.
3. Subject is considered reliable and capable of adhering to the DV0004 protocol (eg, able to understand and complete questionnaires, able to use investigational self-injecting device

presentation 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 DV0004 if any of the PA0012 study exclusion criteria are met.

6.3 Withdrawal criteria

Since DV0004 is a substudy of PA0012, all DV0004 withdrawal criteria are captured in the PA0012 protocol. There are no additional DV0004-specific withdrawal criteria beyond those that are described in PA0012. Subjects are free to withdraw from DV0004 at any time, without prejudice to their continued care. Subjects who withdraw from DV0004 but remain eligible for PA0012 (ie, subjects who have a medical condition or personal preference that precludes further self-injection) may continue in PA0012. These subjects must perform an SFU telephone call 1 week after their last self-injection in DV0004.

Subjects who are withdrawn from bimekizumab treatment during DV0004 will also be required to follow the PA0012 withdrawal procedures.

7 INVESTIGATIONAL MEDICINAL PRODUCT AND INVESTIGATIONAL DEVICE

In the DV0004 substudy, the term IMP refers to the bimekizumab drug product. The term investigational self-injecting device presentation refers to 2 different investigational self-injecting device presentations (bimekizumab-SS-1mL and bimekizumab-AI-1mL) that are comprised of drug product (IMP) associated with a functional secondary packaging.

7.1 Description of device presentations

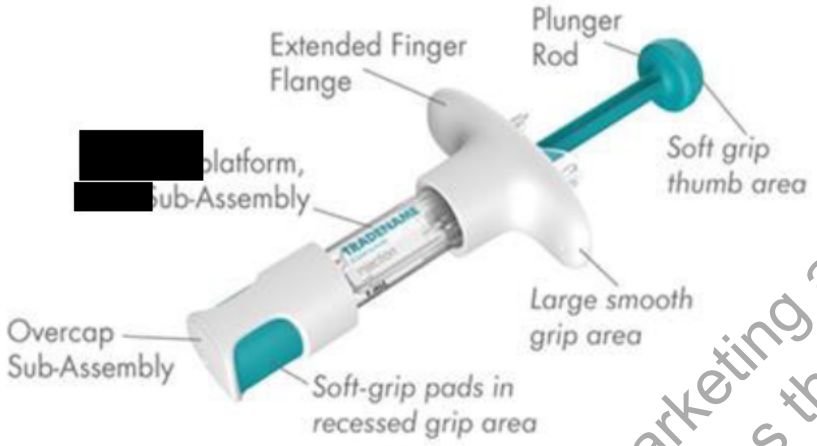
At DV0004 Baseline, each subject will be provided with self-injection training and the IFU for the appropriate device presentation.

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 [redacted] 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 [redacted] safety syringe is a single-use platform device with a passive needle stick safety mechanism. To enhance the device usability, UCB has customized the external [redacted] components including adding an over-cap and modifying the extended finger flange and plunger rod.

Figure 7-1: Bimekizumab-SS-1mL



bimekizumab-SS-1mL=1mL bimekizumab safety syringe

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. 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 4), the bimekizumab-SS-1mL device will be used to administer 160mg injections of bimekizumab. To use the bimekizumab-SS-1mL, the over-cap 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. 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 4), the bimekizumab-AI-1mL devices will be used to administer 160mg injections of bimekizumab. 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 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 nominal formulation of 160mg/mL in 55mM sodium acetate, 220mM glycine, and 0.04% polysorbate 80 at pH 5.0 for sc injection in the bimekizumab-SS-1mL or the bimekizumab-AI-1mL device presentations.

The IMP will be administered according to the schedule shown in Table 5–1 and Table 5–2. Subjects will be assigned to the use of 1 device presentation and will receive 160mg bimekizumab Q4W. Subjects will perform self-injection with the assigned device only at Baseline and at Week 4.

The device presentations 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 PA0012 and reported ADEs and device deficiencies will be assessed within DV0004.

7.3 Packaging

The site will receive uniquely-numbered device presentations (bimekizumab-SS-1mL and bimekizumab-AI-1mL) for use in the DV0004 substudy.

7.4 Labeling

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

The Investigator or hospital pharmacist is responsible for the appropriate storage and accountability of the device presentation 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 presentation 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 device presentations will be supplied to the investigational site. Details of any loss of the self-injection device presentations 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 device presentations 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 (see Section 11.1.1.3) 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 device presentations 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 (self-administration) will be performed in the clinic and observed by the Investigator or his/her designee; monitoring subject compliance is therefore not applicable.

7.8 Concomitant medications/treatments

Any specifications given in PA0012 regarding permitted and prohibited concomitant medications must be followed.

7.8.1 Permitted concomitant treatments (medications and therapies)

Unless otherwise specified in PA0012, 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 PA0012, subjects are not permitted to use topical analgesics at the injection site at Baseline or Week 4 in the DV0004 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 PA0012 and in substudy DV0004. This subject number will be used to identify the subject throughout PA0012 and DV0004 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 device presentations. Eligible subjects will be assigned to the device presentations 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.

8 STUDY PROCEDURES BY VISIT

A general overview of the study assessments is provided in Table 5–1 and Table 5–2. Of note, DV0004 and PA0012 will share a common database/eCRF system (including common AE reporting) and a common IRT.

The following visit windows are permitted:

- As in PA0012, 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 DV0004 substudy, ±3 days.

8.1 Treatment Period

The DV0004 substudy will include all PA0012 study assessments from Baseline to Week 4 (inclusive). All study procedures and assessments will be performed in accordance with Table 5–1 and Table 5–2.

8.1.1 Unscheduled Visit

At the Investigator's discretion, an Unscheduled Visit may be completed at any time during the study but prior to the SFU Visit, if deemed necessary for the subject's safety and well-being.

At this visit, any of the following assessments may be performed, depending on the reason for the visit:

- Record concomitant medication
- Record AEs
- If medically indicated, other assessments that are performed in PA0012 may be performed

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 injection site pain

A VAS will be used to assess overall injection pain due to self-injection at Baseline and at Week 4. 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). The subject will complete the VAS prior to completion of the post-injection SIAQ (refer to Section 9.1 for details).

9.2 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 Baseline and the post-injection SIAQ will be completed within 30 minutes after each self-injection (ie, at Baseline and Week 4).

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,

Question11 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.

9.3 Evaluation of post-use structural, mechanical, and functional integrity of self-injecting device presentations

Visual inspection of the used bimekizumab-SS-1mL and bimekizumab-AI-1mL devices will be performed by appropriately trained site staff to check for any signs of compromised structural or mechanical integrity (ie, clear evidence of damage, such as cracks or loose parts, and not any superficial, cosmetic imperfections, such as scratches or smudges, which have no impact on structural or mechanical integrity). Any device with compromised structural or mechanical integrity will be returned to UCB for further evaluation. The bimekizumab-SS-1mL and bimekizumab-AI-1mL have a lockout feature, which is activated upon completion of the injection and which ensures the needle guard is in position permanently to prevent post-use needle stick injuries. Devices determined to not have the lockout feature in place, as detailed in the IMP Handling Manual, will be packaged and returned to UCB for further evaluation.

10 ASSESSMENT OF PHARMACOKINETIC AND IMMUNOLOGICAL VARIABLES

Blood samples for measurement of trough bimekizumab PK and anti-bimekizumab antibodies (Section 4.1.3) will be collected at the time points specified in the schedule of study assessments (Table 5–1 and 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 in PA0012). 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 PA0012). Detailed information on sample analysis will be provided in a bioanalytical report.

11 ASSESSMENT OF SAFETY

11.1 Adverse events (device presentations)

All AEs (including serious adverse events [SAEs]) will be reported in a common database for PA0012 and DV0004, but only ADEs, SADEs, and device deficiencies will be summarized in the DV0004 substudy. Specifically, only those AEs related to the use of the device presentations 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 device presentations will be summarized separately in the report for the main study, PA0012, please refer to the PA0012 protocol for information on reporting and recording AEs (including SAEs).

11.1.1 Definitions (device presentations)

11.1.1.1 Adverse device effect (device presentations)

An ADE is an AE related to the use of a device presentation. 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.
- Adverse event that is a result of a use error or intentional misuse of the device presentation.

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 this 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.)

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 device presentation.

11.1.1.3 Device deficiency (device presentations)

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 device presentation 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/IEC 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 device presentation is reported (even if the device presentation 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 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 (see Section 7.6).

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 presentation 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.

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 PA0012 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 presentations 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 device presentations.

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).

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

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 device presentation 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 PA0012.

As appropriate for the stage of development and accumulated experience with the IMP and the device presentation, 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 DV0004 substudy. The vital sign assessments presented in Table 5–2 will be captured as part of the PA0012 study and are described in the PA0012 protocol.

12 EFFICACY ASSESSMENTS FOR PA0012

No efficacy assessments will be performed for the DV0004 substudy. The efficacy assessments presented in Table 5–2 will be captured as part of the PA0012 study and are described in the PA0012 protocol.

13 STUDY MANAGEMENT AND ADMINISTRATION

13.1 Adherence to protocol

The Investigator should not deviate from the DV0004 protocol or the PA0012 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 missing information. The Investigator(s)/institution(s) will permit direct access to source data/documents for study-related monitoring, audits, IRB/IEC 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, electrocardiogram (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 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.

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 presentation 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/IEC 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 used or unused IMP and other material in accordance with UCB procedures for the study.

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 device presentations. 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 device presentations have been processed and reported in compliance with the planned arrangements, the protocol, investigational site, and IRB/IEC 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).

14.1 Definition of analysis sets

Two different Safety Sets (SS) will be generated (1 for each device presentation): 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-injecting device presentations. 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 presentation): 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 different Pharmacokinetic Sets (PKS) will be generated (1 for each device presentation): 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 PA0012 feeder studies as in the DV0004 substudy and who have at least 1 evaluable PK assessment in the DV0004 substudy. Pharmacokinetic variables will be analyzed using the PKS-s and PKS-a.

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 presentation 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 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.

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 presentation at Week 4. 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 presentation overall 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 presentation at Baseline (the first self-injection visit, immediately after training in self-injection technique). 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 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 presentation-specific population (PKS-s or PKS-a). Data will be analyzed overall for each device presentation by injection type (self-administered or study personnel-administered), by injection site (abdomen or thigh), by anti-bimekizumab antibody status, 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 bimekizumab PK trough levels and anti-bimekizumab antibodies, blood samples will be taken before self-injection at the Baseline Visit (PK trough and anti-bimekizumab antibody analysis), Visit 2 Week 4 (PK trough analysis only), and Week 8 of PA0012 (PK trough and anti-bimekizumab antibody analysis). Anti-bimekizumab antibody status at or prior to the PK sampling (at Baseline, Week 4, and Week 8) will be used. The number and percentage of anti-bimekizumab antibody-positive and -negative subjects before self-injection (Baseline) and after self-injection (Week 8 of PA0012) will be summarized.

Bimekizumab PK trough levels associated with injection by study personnel using the 1mL PFS (in PA0010 or PA0011) will be analyzed from the pre-injection PK sample collected at Baseline. Bimekizumab PK trough levels associated with subject self-injection using the assigned self-injecting device presentation will be analyzed from the pre-injection PK samples collected at Week 4 and Week 8 (of PA0012).

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.

14.5 Planned safety analyses

The safety variable is the occurrence of ADEs; additional safety and tolerability variables will be collected in PA0012 (see Section 4.1.3.4). Analyses of safety data will be done separately for each device presentation overall and within each device presentation 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 Medical Dictionary for Regulatory Activities v19.0. 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 DV0004 substudy.

14.7 Handling of protocol deviations

Important protocol deviations are deviations from the protocol which could potentially have a meaningful impact on the primary objective of the study. The criteria for identifying important protocol deviations and the classification of important protocol deviations will be defined within the project Data Cleaning Plan. 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 DV0004 substudy.

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 PA0012 feeder studies (PA0010 and PA0011), DV0004 will recruit all subjects who complete the PA0010 and PA0011 feeder studies (including those treated with a comparator or placebo in the feeder study) up to a total of about 200 subjects. A total of 100 subjects (50 subjects per device presentation arm) are planned for PK trough level analyses, but these analyses will only be performed on subjects who were treated with bimekizumab 160mg Q4W (ie, not with placebo or comparator) in the feeder studies prior to rolling over into the DV0004 substudy. The DV0004 substudy will enroll approximately 200 subjects (to compensate for subjects treated with placebo or comparator) to ensure that 100 subjects with stable (160mg Q4W bimekizumab) PK trough levels are available for PK trough analysis.

Subjects who enroll in the DV0004 substudy will be randomly assigned to the bimekizumab-SS-1mL or the bimekizumab-AI-1mL device presentation arms (each device presentation arm will consist of approximately 100 subjects). Within each device presentation 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.

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 and by the person who conducted the informed consent discussion (Investigator or designee). The subject must receive a copy of the signed and dated ICF. As part of the consent process, each subject must consent to direct access to his/her medical records for study-related monitoring, auditing, IRB/IEC 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/IEC 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 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 and Independent Ethics Committees

The study will be conducted under the auspices of an IRB/IEC, 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/IEC, 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/IEC for its review and approval.

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

The Investigator will also promptly report to the IRB/IEC 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/IEC 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/IEC as allowed.

As part of the IRB/IEC requirements for continuing review of approved studies, the Investigator will be responsible for submitting periodic progress reports to the IRB/IEC (based on IRB/IEC 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/IEC following study completion.

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/IEC 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/IEC 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 G. 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.

18 APPENDICES

18.1 Protocol Amendment 1

The main purpose of this protocol amendment was to clarify study procedures and update the description of the IMP.

Modifications and changes

Global changes:

The following changes were made throughout the protocol and are not included in specific changes section:

- The company name was changed from UCB Biopharma SPRL to UCB Biopharma SRL
- The term “legal representative” was deleted from protocol, as it is not applicable to DV0004 or PA00012
- Minor spelling, editorial, and formatting changes were made throughout the document

Specific changes:

Protocol section impacted	Key components of previous protocol text	Key components of revised protocol text	Rationale
Change 1: Administrative section			
Study contact details	[redacted] UCB Celltech Ltd. 208 Bath Road Slough SL1 3WE, UK	[redacted] UCB Celltech Ltd. 208 Bath Road Slough SL1 3WE~~, UK~~ **UNITED KINGDOM**	The country name was added.
	[redacted] ... [redacted]	[redacted] ... [redacted]	The Clinical Project Manager has changed.
	[redacted] UCB BIOSCIENCES Inc. 8010 Arco Corporate Drive Raleigh, NC 27617 UNITED STATES [redacted]	[redacted] UCB ~~BIOSCIENCES Inc.~~ **208 Bath Road** **Slough SL1 3WE** **UNITED KINGDOM** [redacted]	The Clinical Trial Biostatistician has changed.
Change 2: Minor updates to Schedule of study assessments for corresponding visits in PA0012			
Table 5-2	[h] Only subjects affected by enthesitis or dactylitis at Baseline from PA0010 or PA0011. [i] Adverse events not related to the device presentations will be reported in PA0012 and adverse device effects and device deficiencies will be reported in DV0004. A single safety database will be used for both studies.	[h] ~~Only subjects affected by enthesitis or dactylitis at Baseline from PA0010 or PA0011.~~ [i] Adverse events not related to the device presentations will be reported in PA0012 and adverse device effects and device deficiencies will be reported in DV0004. A single safety database will be used for both studies.	Deleted original h footnote since there is no longer a restriction in PA0012 for LDI or LEI assessment to avoid potentially missing data. Analysis for LDI and LEI will still be performed on subjects having dactylitis or enthesitis at Baseline of PA0010 or PA0011. Footnote for adverse events moves from i to h.

Protocol section impacted	Key components of previous protocol text	Key components of revised protocol text	Rationale
Change 3: Update schematic diagram			
Section 5.3, Figure 5-1	**Visit 3, Week 8 (in PA0012)**: • Pre-injection PK sample • Injection by study personnel OR self-injection after training	**Visit 3, Week 8 (in PA0012)**: • Pre-injection PK sample • Injection by study personnel ~~OR self-injection after training~~	IMP administration at Week 8 should be performed by study site staff only.
Change 4: Update description of IMP			
Section 7.2	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 device presentations.	Bimekizumab will be supplied at a ~~concentrat~~ **onnominal formulation** of 160mg/mL ~~(~~**in** 55mM sodium acetate, 220mM glycine, **and** 0.04% polysorbate 80 at pH 5.0~~)~~ for sc injection in the bimekizumab-SS-1mL or the bimekizumab AI 1mL device presentations.	Updated to be consistent with other studies in bimekizumab clinical development program.

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

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.

Approval Signatures

Name: DV0004-protocol-amend-1

Version: 1.0

Document Number: CLIN-000153547

Title: DV0004 Protocol Amendment 1

Approved Date: 19 May 2020

Document Approvals	
Approval Verdict: Approved	Name: [redacted] Capacity: Clinical Date of Signature: 18-May-2020 21:04:01 GMT+0000
Approval Verdict: Approved	Name: [redacted] Capacity: Subject Matter Expert Date of Signature: 19-May-2020 08:07:29 GMT+0000
Approval Verdict: Approved	Name [redacted] Capacity: Medical Date of Signature: 19-May-2020 16:01:08 GMT+0000